Southern African Journal of HIV Medicine
ISSN: (Online) 2078-6751, (Print) 1608-9693

Rapid review of gender-affirming healthcare for children and adolescents: Evidence synthesis (2021–2025) and recommendations for South Africa

Check for updates

Authors:
Ingrid Lynch[1]
KL Dunkle[2,3]
Chris McLachlan[4,5]
Pierre Brouard[2]
Landa Mabenge[6]
Sakhile Msweli[7]
Liberty Matthyse[8]
Marion Stevens[9]
Robin Dyers[10,11,12]
Jenna-Lee de Beer-Procter[13]
Kevin Adams[14]
W.D. Francois Venter[15]
Elma de Vries[16]

Affiliations:
[1]Department of Critical Studies in Sexualities and Reproduction, Rhodes University, Makhanda, South Africa

[2]Centre for Sexualities, AIDS and Gender, University of Pretoria, Pretoria, South Africa

[3]Hubert Department of Global Health, Emory University, Atlanta, United States

[4]KwaZulu-Natal Department of Health, Pietermaritzburg, South Africa

[5]Department of Psychology, University of South Africa, Pretoria, South Africa

[6]Division of Public Health Medicine, School of Public Health, University of Cape Town, Cape Town, South Africa

[7]KwaZulu-Natal Department of Health, Empangeni, South Africa

[8]Gender DynamiX, Cape Town, South Africa

Read online:
Scan this QR code with your smart phone or mobile device to read online.

Background: Since the publication of the Southern African HIV Clinicians Society Gender-Affirming Healthcare (GAHC) Guideline in 2021, global evidence on care for transgender and gender-diverse (TGD) youth has expanded. An updated, locally grounded, evidence-informed assessment of health outcomes can support South African stakeholders, particularly as both adolescents and TGD persons are populations of relevance to HIV prevention, sexual health, and integrated healthcare programmes in South Africa.

Objectives: To synthesise global empirical evidence (2021–2025) across psychosocial, endocrine, surgical, policy, and non-medical gender-affirming interventions for TGD youth under 18, with attention to South Africa's social, legal, and health-system, and HIV-service delivery context.

Method: A rapid review was conducted across 12 databases, supplemented by targeted searches for recent systematic reviews. Eligible sources comprised peer-reviewed empirical studies ($N \geq 5$) reporting psychosocial or physical health outcomes of relevant interventions for TGD youth under 18 (or their families), and systematic or grey-literature reviews with reproducible methods. Findings were synthesised narratively by intervention domain.

Results: The review included 200 primary studies, 29 academic systematic reviews, and four grey-literature reviews. Affirming psychosocial interventions were associated with reduced distress, anxiety and suicidality, and improved functioning and belonging. Puberty blockers and hormone therapy produced expected physiological outcomes under specialist care, with generally mild adverse events and stable or improved mental health. Restrictive policies were linked to poorer mental health, while protective policies improved outcomes. Most studies were small, observational, and Global North-focused.

Conclusion: Evidence supports the safety and effectiveness of GAHC for TGD youth. Strengthening affirming care, timely clinical access, and protective policies in South Africa may improve healthcare engagement and support the delivery of integrated adolescent, sexual health, and HIV-related services for TGD youth.

Keywords: gender-affirming healthcare; transgender and gender diverse; transgender health; gender affirmation; psychosocial support; gender-affirming hormone therapy; gender-affirming surgery; South Africa; sexual health; HIV prevention.

What this study adds: This rapid review of evidence indexed January 2021 to August 2025 indicates that GAHC for TGD youth improves well-being, reduces psychological distress, prevents harm, and supports healthier developmental and mental-health outcomes. Findings inform South African HIV and sexual health practice and policy. This review updates the evidence underpinning the GAHC Guideline and provides clinically relevant evidence for multidisciplinary teams delivering HIV, sexual, reproductive, and adolescent healthcare services.

Introduction

Transgender and gender-diverse (TGD) is an umbrella term referring to people whose current gender identities do not align with the sex assigned to them at birth.[1] Adolescents within this group experience some of the greatest barriers to accessing healthcare globally.[2] In South Africa, research has documented a high prevalence of HIV among transgender women,[3] substantial

[9]Department of Political Science, Stellenbosch University, Stellenbosch, South Africa

[10]Division of Health Systems and Public Health, Department of Global Health, Stellenbosch University, Cape Town, South Africa

[11]WHO-FIC Collaborating Centre, Burden of Disease Research Unit, South African Medical Research Council, Cape Town, South Africa

[12]Department of Health and Wellness, Western Cape Government, Cape Town, South Africa

[13]Department of Psychology, Stellenbosch University, Stellenbosch, South Africa

[14]Division of Plastic, Reconstructive and Maxillo-Facial Surgery, Faculty of Health Sciences, University of Cape Town, Cape Town, South Africa

[15]Wits Ezintsha, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, South Africa

[16]School of Medicine, Faculty of Health Sciences, Nelson Mandela University, Gqeberha, South Africa

Corresponding author:
Elma de Vries,
elma.devries@mandela.ac.za

Dates:
Received: 23 Dec. 2025
Accepted: 02 Apr. 2026
Published: 28 Aug. 2026

How to cite this article:
Lynch I, Dunkle KL, McLachlan C, et al. Rapid review of gender-affirming healthcare for children and adolescents: Evidence synthesis (2021–2025) and recommendations for South Africa. S Afr J HIV Med. 2026;27(1), a1800. https://doi.org/10.4102/sajhivmed.v27i1.1800

healthcare access barriers for TGD people,[4,5] and evidence that access to gender-affirming hormone therapy (GAHT) is associated with improved engagement across the HIV continuum of care, including viral suppression.[6] The National Strategic Plan for HIV, TB and STIs 2023–2028 identifies both adolescents and TGD persons as priority populations for interventions, and calls for the inclusion of gender-affirming services across all levels of care.[7]

Since publication of the 2021 Southern African HIV Clinicians Society (SAHCS) Gender-affirming Healthcare (GAHC) Guideline,[8] the evidence base on GAHC for children and adolescents has expanded substantially. This body of literature spans a wide range of study designs, scopes, and quality, and has been generated predominantly in Global North settings. In parallel, numerous systematic reviews,[9,10,11,12,13,14,15,16,17,18,19,20,21,22,23,24,25,26,27,28,29,30,31,32,33,34,35,36] evidence syntheses,[37,38,39,40] and updated international clinical guidelines[1,41,42,43,44,45] have been released. Taken together, these developments underscore a pressing need among South African stakeholders – including TGD youth, their families and caregivers, educators, mentors, and clinicians – for a comprehensive, rigorous, and transparent synthesis of emerging evidence that is interpreted through local constitutional, historical, and socio-cultural commitments. These commitments shape health policy, clinical practice, and rights-based care in South Africa, including constitutional protections for gender identity as affirmed through equality jurisprudence.[46,47,48] While global debates are often shaped by political and cultural dynamics specific to the Global North,[49,50,51,52,53] South Africa must assess emerging evidence in relation to its own constitutional and public health frameworks, including the principles of Ubuntu, Batho Pele, equity, and collective well-being.[54,55,56] Moreover, the South African context is shaped by health system inequities – including medication stock-outs, provider shortages, and the concentration of services in urban tertiary centres – that affect access to and continuity of care.[4,57,58,59] These constraints are critical to interpreting the global evidence base within South Africa.

The conceptualisation of this review arose through collaboration between the SAHCS, as custodians of the 2021 GAHC Guideline[8]; original authors of the Guideline; Gender DynamiX, a South African transgender advocacy organisation that partnered in developing the Guideline; and the Professional Association for Transgender Health South Africa (PATHSA), which was formed in 2020. PATHSA endorsed the Guideline in 2021 as a professional body supporting the development and stewardship of GAHC practice in South Africa.

This independent rapid review synthesises research indexed from 01 January 2021 to 14 August 2025 to evaluate whether new evidence supports updates to or refinements of the 2021 SAHCS GAHC Guideline.[8] Its overall aim is to collate findings from recent empirical research to support evidence-informed South African clinical practice and the development of a future guideline intended to supersede the 2021 SAHCS GAHC Guideline. The review was conducted by a gender and sexually diverse South Africa-based team with methodological, clinical, and lived-experience expertise. This perspective informed interpretation of retrieved evidence through an equity-oriented, rights-based, and context-sensitive lens. Full partnership with knowledge users strengthens evidence synthesis[60] by ensuring that analyses engage with realities of unequal access, historical trauma, and structural barriers that characterise healthcare experiences for many TGD young people in South Africa.[4,5,6,61,62]

Objectives

The review sought to:

- Synthesise global empirical evidence indexed between January 2021 and August 2025 across all types of GAHC interventions for TGD youth under 18, with attention to both benefits and potential harms.
- Assess the alignment between emerging evidence and the 2021 SAHCS GAHC Guideline, identifying where new findings support, refine, challenge, or extend existing recommendations.
- Interpret global findings within South Africa's constitutional, health-system, and socio-cultural context, including historical inequities and intersecting structural barriers – such as poverty, violence, stigma, racism, sexism, xenophobia, homophobia, transphobia and

Copyright: © 2026. The Authors. Licensee: AOSIS. This work is licensed under the Creative Commons Attribution 4.0 International (CC BY 4.0) license (https://creativecommons.org/licenses/by/4.0/).

Note: Additional supporting information may be found in the online version of this article as Online Appendix 1.

cisnormativity – that shape health risks, access to care, and lived experience.

In doing so, this rapid review aims to support healthcare providers, policymakers, educators, civil society, and families in delivering care that is evidence-informed, developmentally appropriate, and aligned with the rights and dignity of TGD youth.

Research methods and design

A rapid review approach was adopted to balance methodological rigour with timeliness.[60,63,64] Rapid reviews apply systematic review principles while streamlining elements such as screening processes and data extraction to produce timely, policy-relevant evidence within constrained timeframes.[63] This approach was selected to inform planned updates to the 2021 GAHC Guideline while maintaining transparency and analytic integrity. To enhance relevance to clinical practice and lived realities, the author team comprised TGD community members, clinicians who care for TGD youth, and guideline developers and implementers, whose combined expertise informed methodological decisions and interpretation of findings.[60]

The search protocol was developed to reflect the following *a priori* aims, with each domain assessed for all reported outcomes, including both benefits and risks, and with openness to additional categories of intervention emerging inductively from the literature:

- **Psychosocial and supportive interventions:** What is the emerging evidence on psychosocial interventions for TGD youth under 18, including different approaches to mental healthcare, peer or community support, family and parental/caregiver support or lack thereof, and school-based interventions?
- **Endocrine interventions:** What is the emerging evidence on endocrine interventions for TGD youth under 18, including puberty-pausing medication, GAHT, and other endocrine therapy?
- **Surgical interventions:** What is the emerging evidence on gender-affirming surgeries for TGD youth under 18, including masculinising chest surgery and other relevant procedures?
- **Legal, policy, and structural environments:** What is the emerging evidence on the health impacts of legal, policy, systemic and structural interventions shaping GAHC for TGD youth under 18?

Eligibility criteria

Included publications:

- Peer-reviewed primary studies ($N \geq 5$) reporting psychosocial or physical health outcomes of interventions for TGD youth (< 18), including interventions involving family systems, caregivers, educators, or broader public environments.
- Systematic, scoping, and narrative reviews with transparent, reproducible search and screening protocols.
- Grey-literature systematic reviews meeting equivalent methodological standards.
- Studies reporting family-level outcomes, where data specific to TGD youth were disaggregated and presented.

Excluded publications:

- Non-empirical publications, including reviews without published and reproducible protocols, commentaries, think pieces, editorials, and opinion pieces.
- Studies without psychosocial or physical health outcome data for TGD youth (< 18). Proxy-reported data from families or healthcare providers were permitted. For studies of sexual and gender minority youth, separately analysed data for at least five TGD youth were required.
- Case reports or case series with $N < 5$ were excluded. Composite or hypothetical examples were not counted towards N.

Given the diversity of interventions and outcomes, precise Population-Intervention-Comparator-Outcome-Time (PICOT) criteria could not be predefined. However, inclusion criteria were aligned as closely as possible to these frameworks, as shown in Table 1.[65]

All empirically assessed psychosocial and health outcomes and all empirical study designs (quantitative, qualitative, and mixed methods) were eligible. Meta-analysis was not feasible because of extreme heterogeneity in populations, interventions, and outcome measures; findings are therefore synthesised narratively. The full technical report, available at https://pathsa.org.za/resources/rapid-review-2025, adheres to Preferred Reporting Items for Systematic reviews and Meta-Analysis (PRISMA) 2020 reporting standards,[66] with transparently reported streamlining adaptations consistent with interim published guidance for rapid reviews.[64]

TABLE 1: PICO(T) map of eligibility criteria for included studies.

Domain	Criteria
Population	TGD youth under 18 years old ***or*** family units including TGD youth under 18 years old. Minimum $N = 5$.
Intervention and/or exposure	Any type of psychosocial or medical care, support, policy, practice or deliberate harm delivered to or targeting TGD youth under age 18 years across all socioecological levels (individual, dyadic and/or familial, institutional, policy and/or legal, sociocultural).
Comparator and/or control	Any or none (not required).
Outcomes	Any empirically assessed health or psychosocial outcome(s).
Time	Any follow-up time frame allowed, including both prospective or retrospective assessment.
Study types	Quantitative, qualitative, mixed-methods, including prospective and retrospective designs. Systematic reviews eligible if based on transparent, reproducible search and screening protocols.

PICO(T), Population-Intervention-Comparator-Outcome-Time; TGD, transgender and gender-diverse.

Search strategy, screening and selection

Searches were conducted on 26 November 2024, 04 December 2024, and 14 August 2025 across 12 databases via EBSCOhost (University of Pretoria), supplemented by searches of ClinicalTrials.gov and the International Standard Randomised Controlled Trial Number (ISRCTN) registry, and targeted searches for recent systematic reviews. Search date limits were set to capture records indexed between 01 January 2021 and 31 December 2025, thereby including articles indexed online ahead of their recorded publication dates. The search strategy combined [any term for trans and gender diverse identity] AND [any term for youth under 18] AND [any term for interventions related to gender identity]. Full search strings are provided in the technical report. No language restrictions were placed on the search results. Titles and abstracts of non-English sources were screened based on publisher-provided English translations whenever available and supported by Google Translate as needed.

Data extraction and analysis

Two custom Airtable-based tools were used to extract data from primary studies and systematic reviews, capturing study characteristics, populations, interventions, outcomes, and key results. Data extraction for non-English sources was based on publisher-provided English translations in all but one case, where the full text of a Spanish-language article was translated using Google Translate. The machine-translated text was reviewed alongside the original article, with key passages verified by a Spanish-speaking research assistant. Formal *de novo* risk-of-bias or certainty grading across all individual studies was not undertaken; instead, where available, methodological appraisals and certainty assessments reported in included systematic reviews were used qualitatively to inform interpretation.

Data extraction from full-text sources was conducted by authors KL Dunkle and Ingrid Lynch. Two large language models (LLMs), ChatGPT and Perplexity, were used in a limited, supportive capacity. A structured data-extraction prompt was applied to individual PDFs to generate draft plain-text data extraction elements aligned with predefined Airtable fields. These drafts were line-checked against the original sources, corrected where necessary, and manually entered the extraction database. LLMs were instructed to flag missing, ambiguous, or uncertain data elements for targeted human review, and all errors and gaps were resolved by the human reviewers using the original reports.

LLMs were also used on an *ad hoc* basis to cross-check draft narrative descriptions of results against spreadsheets of the extracted data and source PDFs, supporting identification of potential omissions or internal inconsistencies for human correction. LLMs were not used for study screening, inclusion–exclusion decisions, formal analysis, recommendation development, conflict-of-interest statements, or contextual framing. All LLM-generated outputs were treated as provisional drafts and were reviewed, verified, and rewritten by the human author team prior to inclusion.

Narrative synthesis of findings

Narrative syntheses drew on structured Airtable data extractions, with attention to intervention type, outcome measures, study design, sample characteristics, follow-up duration, and any certainty ratings reported in prior reviews. Findings were organised across five domains of care: psychosocial, endocrine, surgical, non-medical gender-affirming practices, and policy and legal interventions. Domain leads verified that narrative summaries accurately reflected underlying data and appropriately characterised any methodological uncertainty. The synthesis prioritised practice-relevant findings and patterns in relation to benefits, harms, and equity and access considerations, while explicitly noting where evidence was sparse, methodologically weak, or inconsistent.

Three cross-cutting interpretive lenses guided synthesis:

- Global scope and local gaps, highlighting where South African/Global South evidence remains absent.
- Equity and context, examining whether and how studies addressed intersecting axes of inequality.
- Policy and practice relevance, focusing on implications for South African clinicians, families, policymakers, and guideline developers.

Finally, to strengthen practice relevance, synthesised findings were assessed against the 2021 SAHCS GAHC Guideline.[8] For each intervention domain, evidence was considered in terms of direction of effect, consistency, methodological quality, follow-up duration, and relevance to the South African context. Implications for existing Guideline recommendations were classified as:

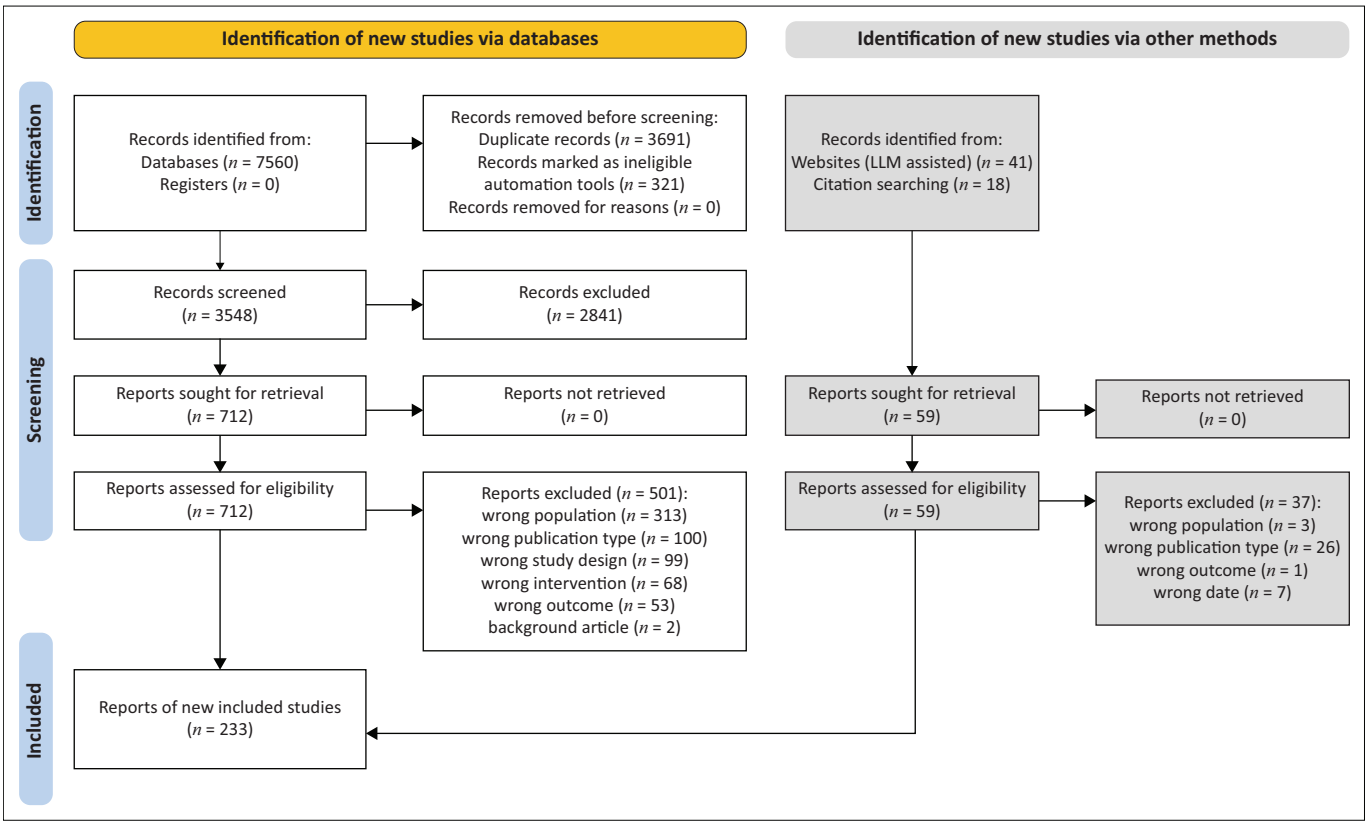
- Consistent – emerging evidence aligns with current guidance.
- Refine – emerging evidence suggests that current guidance could be sharpened or made more specific.
- Challenge – emerging evidence contradicts current guidance or introduces caveats.
- New content area – emerging evidence highlights an area not addressed in current guidance.

These classifications were reviewed iteratively by the full author team, with reference to the synthesised evidence, to ensure analytic coherence and contextual appropriateness.

Results

The final dataset comprised 200 primary studies, 29 academic systematic reviews, and four grey-literature systematic reviews, yielding 233 included sources.

The PRISMA diagram (Figure 1) details the identification, screening, and inclusion process, including duplicate removal, automated exclusions of ineligible publication types, and abstract and full-text screening.[66,67]



Source: Preferred Reporting Items for Systematic reviews and Meta-Analysis extension for Scoping Reviews (PRISMA) diagram created by the authors, following PRISMA 2020 guidelines

Note: Please see the full reference list of Lynch I, Dunkle KL, McLachlan C, et al. Rapid review of gender-affirming healthcare for children and adolescents: Evidence synthesis (2021–2025) and recommendations for South Africa. S Afr J HIV Med. 2026;27(1), a1800. https://doi.org/10.4102/sajhivmed.v27i1.1800.

LLM, large language model.

FIGURE 1: PRISMA diagram showing flow of literature searches, exclusions and inclusions of retrieved sources.

The complete list of primary studies and systematic reviews, along with extracted data, is provided in the Online Supplementary Appendix (Table S-A and Table S-B).

Overall, 108 of the 200 included primary studies had been described in at least one systematic review in our dataset. We also retrieved 92 primary research articles that were *not* included in any of the prior systematic reviews identified here. The inclusion of these 92 studies increases the primary literature base considered in this report by 85.2% relative to that synthesised in the retrieved review literature. Table S-C in the Online Supplementary Appendix maps each primary study to the systematic review(s) in which it appeared and reports formal certainty appraisals, where available. For studies included in multiple reviews, certainty assessments varied according to the research questions and methods applied in each review; notes and critiques on how these were conducted appear in Table S-B and Table S-C (see Online Supplementary Appendix).

In the remainder of our analyses, prior systematic reviews were treated as evidence sources in their own right and used qualitatively to contextualise patterns and the certainty of evidence in the primary studies; however, care was taken to avoid over-emphasising primary studies appearing in multiple reviews. Synthesis and conclusions are grounded in the full source dataset, with insights from prior reviews informing interpretation rather than driving analysis.

Psychosocial interventions and support

We identified 53 primary studies,[68,69,70,71,72,73,74,75,76,77,78,79,80,81,82,83,84,85,86,87,88,89,90,91,92,93,94,95,96,97,98,99,100,101,102,103,104,105,106,107,108,109,110,111,112,113,114,115,116,117,118,119,120] 12 academic systematic reviews,[10,11,13,15,19,20,22,23,24,31,36,121] and three grey-literature systematic reviews[37,38,39] examining psychosocial aspects of care for TGD children and adolescents. The full list of primary studies is provided in Table S-D in the Online Supplementary Appendix. The evidence base is methodologically heterogeneous and dominated by observational and qualitative designs, with the majority comprising cross-sectional surveys or retrospective clinic-based analyses.[72,76,77,85,91,92,93,94,96,99,100,102,103,104,106,108,109,112,113,117,118,119,120] A substantial proportion of studies used qualitative or mixed methods designs, drawing on interviews with young people, caregivers, families, or clinicians to explore experiences of support, identity development, barriers to access, and care processes.[70,79,80,84,87,88,90,93,98,101,105,110,111,114]

Affirming psychosocial practices such as supporting a young person's gender expression,[19,69,83,89,91,93,94,115,117] strengthening family and peer connectedness,[10,22,36,76,81,85,92,104,106,109] creating safer school environments,[11,36,86,93,95,100,102,108,113,118,121] and providing tailored psychological or digital interventions[37,68,71,73,74,75,79,120] are associated with reductions in depression, anxiety, and suicidality, as well as improvements in resilience, sense of belonging, school participation, and daily functioning.

However, access to affirming support is not evenly distributed, with nonbinary youth and racially marginalised TGD youth reporting lower levels of gender affirmation and support across social and care contexts.[91,104] No included study or systematic review reported harms attributable to affirming psychosocial care.

By contrast, non-standard or pathologising practices – including identity-change efforts, enforced or non-clinical delays in social affirmation, or withholding affirmation – which fall outside recognised standards of psychosocial care, are consistently associated with adverse outcomes, including heightened distress, self-harm, suicidality, and deteriorating family relationships.[38,77,87,94,111]

Most studies are cross-sectional, self-reported, and concentrated in high-income settings, with relatively few longitudinal or experimental designs; these factors limit certainty of evidence in individual reports. Nonetheless, the consistency of findings across survey-based, qualitative, and mixed-methods studies, alongside diverse care contexts and outcome measures, supports psychosocial affirmation as both safe and beneficial. Taken together, findings underscore that mental health outcomes are shaped by family, school, and community contexts, and highlight the importance of supporting children and adolescents who face inconsistent or unsupportive family environments. Findings also point to the need to support youth facing overlapping social and structural stressors, and to ensure equitable access to affirming psychosocial support across diverse social, educational, and community settings.

Overall, the evidence on psychosocial interventions and support for TGD youth is consistent with the 2021 SAHCS GAHC Guideline recommendations. Table 2 summarises key implications for guideline development, mapping synthesised evidence against existing guidance and highlighting areas of support and refinement.

Endocrine interventions

We identified 23 primary studies,[122,123,124,125,126,127,128,129,130,131,132,133,134,135,136,137,138,139,140,141,142,143,144] three academic reviews,[26,28,33] and one grey-literature report[39] with focused evaluation of puberty-pausing medication; 28 primary studies,[145,146,147,148,149,150,151,152,153,154,155,156,157,158,159,160,161,162,163,164,165,166,167,168,169,170,171,172] and two academic reviews[25,32] with focused evaluation of GAHT; and 53 primary studies,[78,87,88,153,154,155,156,173,174,175,176,177,178,179,180,181,182,183,184,185,186,187,188,189,190,191,192,193,194,195,196,197,198,199,200,201,202,203,204,205,206,207,208,209,210,211,212,213,214,215,216,217,218,219,220] 11 academic reviews[9,11,12,16,17,18,21,27,29,34,35] and three grey-literature reports[37,38,40] with joint or overlapping evaluation of puberty pausers and GAHT (see Online Supplementary Appendix: Table S-E, Table S-F and Table S-G).

The literature shows a consistent pattern: endocrine interventions for TGD adolescents generally achieve their intended physiological effects[25,32,33,37,38,40,124,126,203]; adverse events are typically anticipated, predominantly mild, and manageable under routine monitoring in specialist care, with specific adverse events described in relation to individual interventions below.[123,124,131,146,150,173] Mental-health outcomes are broadly stable or improved.[122,127,142,166,209] Although the evidence base is methodologically constrained and concentrated in high-income clinical settings, available data provide a short- to medium-term picture of effectiveness and safety.[9,21,27,34,35]

TABLE 2: Summary of evidence and guideline implications for psychosocial care (2021–2025).

Domain	Recommendation (SAHCS 2021)	Implication (2021–2025 evidence)
1. Informed consent	For children under 12, consent from parents/guardians with child assent; for adolescents ≥ 12, participatory consent involving adolescent and caregiver(s); disclose risks/benefits.	**Consistent →** Evidence supports consent as a youth-centred, affirming process. **Refine →** Emphasise neurodiversity- informed adaptations (clear structure, accessible communication).
2. Social transition	Affirmed names, pronouns, clothing, and gender expression should be supported when requested; processes should be discussed with families/schools.	**Consistent →** Evidence shows strong protective effects of affirmation, stability of early transitions, and harms when support is delayed. **Refine →** Emphasise that both childhood and adolescent transitions are safe when affirmed, and that additional support might be required in hostile school or community environments.
3. Family involvement	Family participation improves outcomes; interventions may include psychoeducation, counselling, and resource-linking for caregivers and extended family.	**Consistent →** Evidence supports family affirmation as the key protective factor. **Refine →** Emphasise psychoeducation and supportive interventions that help families move through fears/uncertainties, and the importance of proactive safety-planning if family rejection occurs.
4. School and community engagement	MHPs should support TGD youth in navigating schools and communities, advocate for safe and inclusive environments, and provide psychoeducation to stakeholders.	**Consistent →** Evidence reinforces the protective role of inclusive school climates, safe bathrooms, supportive teachers, and access to affirming counselling and confidential school-based spaces. Harms are linked to victimisation and exclusion rather than affirmation.
5. Mental health assessment and support	MHPs should assess/address co-occurring conditions (depression, anxiety, suicidality, ASD) without pathologising identity.	**Consistent →** High rates of distress are linked to victimisation/rejection, not identity. Affirming interventions show benefit. **Refine →** Explicitly recommend autism-informed practices (structured sessions, sensory adaptations) and recognise distress arising from care delays or prolonged waitlists.
6. Affirmation and non-pathologisation	Care must be affirming, non-pathologising, and avoid gatekeeping; centre the adolescent's lived experience.	**Consistent →** Affirmation reduces suicidality and distress, while restrictive or 'watchful waiting' approaches that withhold affirmation cause harm. **Refine →** Emphasise that non-clinical enforced delays undermine well-being and are inconsistent with affirming care.
7. Enabling affirming environments	MHPs should advocate for TGD youth's rights, contribute to policy/institutional reforms, and promote safe environments.	**Consistent →** Supportive family, school, and community environments are strongly protective. **Refine →** Emphasise anticipating minority stress in hostile social environments and the need to address inequities faced by multiply marginalised youth.
8. Contraindicated approaches	Practices such as gender identity and expression change efforts ('conversion therapy'), pathologisation, or non-clinical delays in care are harmful and contraindicated.	**Consistent →** Evidence confirms these practices increase distress, self-harm and suicidality. **Refine →** Explicitly name contraindicated practices.
9. Equity and access	Not explicitly addressed in the 2021 guideline.	**New →** Evidence highlights persistent inequities in affirmation and safety for youth facing intersecting forms of exclusion – including nonbinary young people and those in unsupportive families or schools. Future guidance should explicitly incorporate equity considerations.

MHP, Mental Healthcare Practitioner; TGD, transgender and gender-diverse; ASD, Autism spectrum disorder; SAHCS, South African HIV Clinicians Society.

TABLE 3: Summary of evidence and guideline implications for puberty-pausing medication (2021–2025).

Domain	Recommendation (SAHCS 2021)	Implication (2021–2025 evidence)
1. Indications and eligibility	Offer GnRHa from Tanner stage 2 for adolescents with persistent gender incongruence to relieve dysphoria, prevent unwanted pubertal changes, and support well-being.	**Consistent** → Evidence confirms reliable suppression and short-term safety. **Refine →** Earlier initiation is associated with more favourable physical and psychosocial trajectories; non-clinical delays reduce effectiveness and increase distress.
2. Initiation and consent	Initiate after MDT assessment confirming gender incongruence and capacity for informed consent; adolescents ≥ 12 may consent independently; caregiver involvement encouraged.	**Consistent** → Current MDT-based framework remains appropriate; combined-pathway evidence shows that coordinated endocrine–mental-healthcare supports clearer counselling and smoother decisions about timing and possible GAHT sequencing.
3. Family / caregiver involvement	Collaborative approach improves outcomes; lack of family support should not preclude access.	**Consistent** → Evidence shows that family support enhances well-being. Combined-pathway data suggest better mental-health trajectories when adolescents have family engagement during both PS and GAHT stages, underscoring the importance of family counselling where feasible.
4. Clinical oversight	Care should be managed by paediatric endocrinologist or trained provider using available GnRHa agents.	**Consistent** → Evidence reinforces the need for skilled oversight.
5. Information and counselling	Provide clear information on benefits, risks, and reversibility.	**Consistent** → Evidence supports the importance of clear, anticipatory counselling about expected effects, reversibility, and expected timing of potential subsequent GAHT.
6. Fertility	Counsel before initiation; early suppression can preclude gamete preservation.	**Consistent** → Evidence remains limited but coherent, and supports early, developmentally tailored counselling. Semen and oocyte cryopreservation are feasible and generally safe, but uptake is low due to procedural dysphoria, high cost, and late referral.
7. Monitoring – Psychosocial well-being	Follow-up should include psychosocial monitoring.	**Consistent** → Evidence indicates stable or improved mental health during PS, with no signals of harm. Combined-pathway findings show additional psychological benefit when progression to GAHT is timely and uninterrupted.
8. Monitoring – Bone health and growth	Monitor bone health and growth during follow-up.	**Consistent→** Evidence shows transient BMD reductions (especially lumbar spine) and slowed growth during PS, with recovery after GAHT. **Refine →** Earlier pubertal stage at initiation is linked to more favourable growth and bone-density trajectories, while later initiation and prolonged GnRHa monotherapy may constrain recovery, underscoring the need for DXA monitoring where clinically indicated.
9. Monitoring – Body composition and metabolic indicators	Not explicit in 2021 guideline.	**Refine** → PS increases fat mass and reduces lean mass, which generally normalises after GAHT. Include anticipatory guidance on these expected changes, alongside counselling on physical activity and nutrition to support bone health and cardiometabolic well-being.
10. ASD considerations	Use concrete communication; involve ASD-experienced clinicians.	**Consistent** → No new PS-specific evidence. Maintain guidance.
11. Equity and access	Not explicitly addressed in 2021 guideline.	**New** → Structural barriers (delays, insurance, geographic inequities) affect timing and outcomes. Combined-pathway evidence shows delays between PS and GAHT can worsen mental-health trajectories. Add explicit guidance on equitable access, provincial provision, and appeal pathways.

SAHCS, South African HIV Clinicians Society; GnRHa, Gonadotropin-Releasing Hormone Agonist; MDT, Multi-disciplinary team; GAHT, gender-affirming hormone therapy; PS, Puberty supression; BMD, Bone mineral density; DXA, Dual energy X-ray absorptiometry; ASD, Autism spectrum disorder.

Puberty-pausing medication reliably halts unwanted pubertal development,[39,124,126,130,136,142,143] and GAHT induces expected masculinising or feminising changes.[25,32,37,38,150] Endocrine and metabolic parameters typically remain within clinically acceptable ranges under supervised care.[124,140,150,210] Bone-density reductions during pubertal suppression are common and well-described,[125,132,137,195] and typically show partial or substantial recovery following subsequent GAHT or endogenous puberty, especially when progression to hormones is timely and aligned with clinical indicators.[125,175,197,203,207,213] Serious adverse events are rare across endocrine pathways, with no consistent pattern of irreversible harm.[149,173,204,216,220]

Mental-health outcomes are heterogeneous at the individual level, yet broadly stable-to-favourable across cohorts. Adolescents who access puberty suppression and/or GAHT generally show reductions in depressive symptoms and suicidality, alongside improved appearance congruence and functioning, compared with their own baseline and with peers who want but cannot access treatment.[160,161,164,166,181,194,209] Worsening mental-health trajectories are more consistently associated with delayed or restricted access to care than with endocrine treatment,[166,209] with GAHT linked to lower risks of suicidality-related emergency or inpatient care and to fewer mental-health diagnoses and psychiatric hospitalisations following treatment initiation.[192,200]

Longitudinal data indicate high continuation into adulthood and very low reported regret among adolescents who commence endocrine care.[153,154,156,212,213] Where discontinuation occurs, it is very often linked to external or structural factors (such as access barriers, service disruptions, costs, insurance denials, family stressors, or bullying), completion of desired physical changes, or evolving identity-related needs, rather than to treatment-related side effects or regret.[16,153,154,163,184]

Although menstrual suppression as gender-affirming care is not explicitly addressed in the 2021 SAHCS GAHC Guideline, review of evidence from five primary sources[221,222,223,224,225] (Online Supplementary Appendix: Table S-H) suggests that it is a safe, effective, and highly valued component of care for TGD adolescents who menstruate. Reported outcomes include high rates of amenorrhoea, reduced pain and menstrual-related dysphoria, and high overall satisfaction, with mild and infrequent adverse events.[221,222,223,224,225]

Fertility preservation was addressed in 16 primary sources[226,227,228,229,230,231,232,233,234,235,236,237,238,239,240,241] (Online Supplementary Appendix: Table S-I), one academic systematic review,[30] and two grey-literature reviews.[37,38] Although gamete preservation appears feasible and generally safe for adolescents, interest is typically low, and accessibility for those who are interested is substantially constrained by cost, procedural dysphoria, and timing of referral.[37,38,226,227,229,230,231,232,233,234,235,236,237,238,239,240,241] These factors highlight the importance of early, developmentally appropriate, and iterative fertility counselling.

TABLE 4: Summary of evidence and guideline implications for gender-affirming hormone therapy (2021–2025).

Domain	Recommendation (SAHCS 2021)	Implication (2021–2025 evidence)
1. Indications and eligibility	Initiate GAHT for adolescents with persistent incongruence, desire for hormonal change, and capacity for informed consent.	**Consistent** → Evidence shows GAHT reliably induces intended changes and improves well-being. Combined-pathway evidence shows continuity of benefit when GAHT follows timely PS.
2. Consent	From age 12, competent adolescents may consent independently; partially irreversible effects require careful counselling.	**Consistent** → Maintain detailed counselling. Combined-pathway data reinforces the need to discuss sequencing, timing, and irreversible features.
3. Decision-making	Clinicians and MHPs should confer on readiness; parental input improves outcomes.	**Consistent** → MDT approach remains appropriate. Combined-pathway evidence highlights the value of coordinated endocrine-mental healthcare during transition from PS to GAHT.
4. Timing	Timing should be individualised, considering prior PS, growth potential, family support, and risks of delay.	**Refine** → Structural or administrative delays are associated with worsening mental-health symptoms. Combined-pathway studies indicate improved well-being and social functioning when progression from PS to GAHT is uninterrupted. Service planning should define and support timely access.
5. Regimens (including non-binary care)	Gradual dose escalation in younger adolescents; tailor to goals, including for non-binary youth.	**Consistent** → Goal-based titration remains appropriate. Combined-pathway data show that earlier PS may shape later outcomes (height, hip geometry). Continue supporting flexible dosing for non-binary clients.
6. Fertility	Provide counselling before GAHT on irreversible effects and preservation options.	**Consistent** → Evidence supports early, realistic fertility counselling. Gamete preservation is often feasible when GAHT is paused for several months, but adolescent data remain limited and uptake is low, partly due to cost, procedural dysphoria, and late referral.
7. Contraception	GAHT is not contraceptive; discuss contraception where pregnancy is possible.	**Consistent** → Maintain guidance.
8. Concurrent health needs	Manage co-existing conditions alongside GAHT; do not delay access unnecessarily.	**Consistent** → Evidence supports this approach; there is no evidence that supports delaying GAHT for common concurrent conditions.
9. Monitoring – Bone health and growth	Monitor bone health and growth.	**Refine** → Combined-pathway evidence shows that BMD typically declines during GnRHa and increases after GAHT, with generally favourable long-term recovery, including stronger catch-up on testosterone. Transfeminine adolescents may have persistent lumbar-spine deficits, underscoring the need for ongoing DXA monitoring, adequate oestrogen dosing, vitamin D assessment, and avoidance of prolonged suppression without progression to either GAHT or endogenous puberty, as indicated.
10. Monitoring – Body composition and metabolic indicators	Monitor lipids, glucose, liver enzymes, and other metabolic markers.	**Consistent** → Predictable metabolic shifts occur that are consistent with the affirmed gender and are rarely clinically significant. Combined-pathway data show no additional metabolic safety concerns when transitioning from PS to GAHT.
11. Monitoring – Cardiovascular/ thrombosis	Include cardiovascular risk assessment.	**Consistent** → Adolescents on GAHT do not show new cardiovascular safety signals; thrombotic events are rare. Combined-pathway studies report small QTc changes and transient blood-pressure shifts that remain within normal ranges, including among youth on psychotropic medications.
12. Monitoring – Psychosocial outcomes	Monitor psychosocial well-being and satisfaction.	**Consistent** → Evidence demonstrates improved well-being and high satisfaction during GAHT. Combined-pathway studies show very high continuation, rare regret, and stable or improved mental-health trajectories from PS → GAHT.
13. Equity and access	Not explicit in 2021 guideline.	**New** → Structural inequities (funding, geography, age-based restrictions, service delays) shape treatment timing and outcomes. Combined-pathway findings show that delays between PS and GAHT worsen psychosocial symptoms. Add explicit equity guidance: provincial scaling, public-sector funding, telehealth access, and accountability mechanisms for wait times.

GAHT, gender-affirming hormone therapy; PS, Puberty supression; MHP, Mental Healthcare Provider; MDT, Multi-disciplinary team; GnRHa, Gonadotropin-Releasing Hormone Agonist; DXA, Dual energy X-ray absorptiometry; QTc, corrected QT interval on an electrocardiogram.

TABLE 5: Summary of evidence and guideline implications for menstrual suppression (2021–2025).

Domain	Recommendation (SAHCS 2021)	Implication (2021–2025 evidence)
1. Indication and purpose	Mentioned only as an option when bleeding persists on testosterone or when clients do not wish to use testosterone.	**New** → Evidence shows menstrual suppression functions as a gender-affirming intervention that reduces menstrual-related dysphoria and pain. Recognise suppression as a standalone component of gender-affirming care, not only an adjunct to testosterone.
2. Eligible methods	Leuprolide, medroxyprogesterone acetate, anastrazole may be considered.	**Refine** → High amenorrhoea rates and favourable safety profiles demonstrated across progestin-based methods and LARC (LNG-IUD, etonogestrel implant). Expand recommended evidence-based method options and include expected effectiveness.
3. Counselling and informed consent	No adolescent-specific guidance; general advice only.	**New** → Provide anticipatory, developmentally appropriate counselling on expected bleeding patterns, onset of amenorrhoea, side-effect profiles, and integration with future GAHT or reproductive-health planning. Clarify that menstrual suppression does not impair long-term fertility and may support adolescents who wish to preserve future reproductive options. Address potential dysphoria linked to procedures (e.g. pelvic exams, IUD insertion).
4. Psychosocial outcomes	Not addressed.	**New** → Evidence shows reductions in menstrual-related dysphoria, improved daily functioning, and high satisfaction once amenorrhoea is achieved. Highlight psychosocial benefits in the guideline.
5. Safety and adverse events	Not addressed.	**New** → Evidence shows generally mild, manageable adverse effects and no serious complications. Reinforce routine monitoring and anticipatory side-effect counselling.
6. Equity and access	Not addressed.	**New** → Address access barriers (cost, method availability, procedural discomfort, and variable provider experience with gender-affirming menstrual suppression) to support equitable provision across public-sector services.

SAHCS, South African HIV Clinicians Society; LARC, Long-Acting Reversible Contraception; LNG-IUD, Levonorgestrel Intrauterine Device; GAHT, gender-affirming hormone therapy.

Overall, the evidence aligns with the 2021 SAHCS GAHC Guideline recommendations. Table 3 and Table 4 summarise key implications for guideline development for puberty pausing and GAHT, respectively, mapping synthesised evidence against existing recommendations. Table 5 outlines implications for future guideline development related to menstrual suppression.

Surgical interventions

We identified 10 primary studies reporting outcomes of gender-affirming surgery in adolescents,[242,243,244,245,246,247,248,249,250,251] and 15 primary studies in which surgery was examined within broader gender-affirming care trajectories that also included endocrine and/or psychosocial care[163,184,196,213,228,252,253,254,255,256,257,258,259,260,261] (Online Supplementary Appendix: Table S-J1 and Table S-J2).

TABLE 6: Summary of evidence and guideline implications for adolescent gender-affirming surgery (2021–2025).

Domain	Recommendation (SAHCS 2021)	Implication (2021–2025 evidence)
1. Eligibility and decision-making	Surgical eligibility and decision-making should be determined by a multidisciplinary team, including mental-health professional(s), surgeon(s), the adolescent, and parents/legal guardians.	**Consistent →** All adolescent surgeries in the identified evidence occurred within specialist multidisciplinary services and were embedded in broader GAHC pathways. Outcomes were favourable in these settings. No evidence supports modifying multidisciplinary eligibility processes; findings reinforce the importance of team-based, longitudinal, individualised care.
2. Indications and type of surgery in adolescence	For adolescents, GAS is most commonly limited to masculinising chest reconstruction for those mature enough to require and benefit from surgery; other procedures are usually deferred to adulthood.	**Consistent →** Evidence in minors is almost entirely limited to masculinising chest surgery, with high satisfaction and very low regret in small, mostly single-centre cohorts with low- to very-low-certainty evidence, though point estimates for regret are consistently close to zero. Insufficient data exist to expand adolescent indications, but findings support maintaining access where clinically indicated.
3. Preoperative requirements	Preoperative requirements include a thorough informed-consent process and at least one referral letter from a mental-health provider familiar with gender-affirming healthcare.	**Refine →** Low complication rates, high satisfaction, and very low regret occur in settings where careful assessment and preparation are standard. At the same time, evidence of unmet need and distress from cost, waitlists, and policy restrictions suggests preventing and avoiding non-medical delays beyond those required for safe, well-informed decision-making.
4. Consent	Consent requires the adolescent to be over 12, sufficiently mature, cognitively capable, and legally assisted by a parent/legal guardian. Irreversibility must be emphasised.	**Consistent →** No included studies examined consent processes, and South African legal standards remain unchanged. Current guidance is appropriate, especially as surgery is typically only offered to older adolescents. Emerging evidence affirms the value of clear communication and expectation-setting.
5. Autonomy and well-being	The autonomy and well-being of the adolescent must be respected and central to decisions.	**Refine →** Improvements in dysphoria, body image, daily functioning, and social participation, alongside very low regret, underscore the importance of centring adolescent goals. Evidence that non-clinical delays contribute to distress reinforces balancing caution with respect for adolescents' bodily autonomy through shared decision making that actively incorporates adolescents' stated priorities.
6. Psychosocial support	Comprehensive psychosocial support before and after surgery is strongly recommended; ongoing support is especially important for adolescents with neurodevelopmental or psychological challenges.	**Refine →** Surgery alleviates major sources of distress but does not address broader minority stress or structural barriers. Evidence emphasises structured, ongoing mental-health, family, peer, and school-based support to sustain gains in well-being while addressing ongoing minority stressors.
7. Post-surgical care, safety and complications	Post-surgical care should include psychological support, physiotherapy, and peer/community support resources.	**Refine →** Available cohort and systematic-review evidence from predominantly single-centre, observational studies demonstrates low complication rates in adolescents, with serious events rare and rates comparable to, or lower than, adults or cisgender adolescents undergoing analogous procedures. Guidelines could more explicitly acknowledge this favourable safety profile while reinforcing the need for structured follow-up and ongoing psychosocial care.
8. Equity and access	Access is constrained by limited resources, long public waitlists, and high private-sector costs.	**Refine →** Evidence from cohort and qualitative studies shows structural barriers (cost, geography, waitlists and policy restrictions) drive treatment delays, unmet need and psychological distress. Guidelines could incorporate explicit equity-focused recommendations: reducing non-clinical delays, scaling public-sector capacity, transparent waitlist management, and advocacy for funding and rights-based accountability.

SAHCS, South African HIV Clinicians Society; GAHC, gender-affirming healthcare; GAS, Gender-affirming surgery.

Two grey-literature systematic reviews assessed surgical outcomes in youth.[37,38]

Evidence for patients under age 18 is limited in volume but highly consistent, focusing almost entirely on masculinising chest reconstruction, which is the only gender-affirming surgery routinely accessed by adolescents.[242,243,244,245,246,247,248,249,250,251] A very small number of other procedures (e.g. hysterectomy, vaginectomy, facial feminisation) are reported in United States national registry data, but are vanishingly rare in under-18s.[245] Within multidisciplinary programmes, masculinising chest surgery shows very low complication and revision rates, with safety profiles favourably comparable to those observed in adults or cisgender youth undergoing analogous chest procedures.[242,244,245,249,250]

Psychosocial outcomes of gender-affirming surgery are consistently positive in the short to medium term, including improved body image, reduced dysphoria, and increased participation in social, educational, and physical activities, alongside high levels of patient satisfaction.[37,38,243,247,250,251] Reported regret is rare, including in the few longer-term follow-up studies that are available.[37,247,249,250] Studies examining surgical interventions within broader gender-affirming care trajectories report similarly favourable safety and psychosocial outcomes, reinforcing findings from surgery-specific cohorts.[163,184,196,213,228,252,253,254,255,256,257,258,259,260,261] Adolescents considering or recovering from surgery benefit from ongoing care from multidisciplinary teams, affirming family support, and peer networks.[228,256,259] These findings reinforce the importance of situating surgical interventions within broader trajectories of gender affirmation, including ongoing psychosocial support.

Findings are consistent with the 2021 GAHC Guideline recommendations. Table 6 summarises key implications for guideline development and identifies areas for potential refinement.

Non-medical gender-affirming practices

We identified one large online survey[262] (Online Supplementary Appendix: Table S-K) and one narrative review[14] addressing non-medical gender-affirming practices, including binding, tucking, packing, and padding. Although the evidence base is limited, findings indicate that these practices are meaningful tools through which TGD adolescents manage gender dysphoria, navigate public and social spaces, and feel more at ease in their bodies.[14,262] For many adolescents, these practices are partly driven by limited or delayed access to endocrine and/or surgical GAHC. The available evidence does not indicate serious health risks associated with packing or padding. Physical discomfort related to binding and tucking appears to be common but manageable when TGD youth have access to safer materials and practical guidance.[14,262]

Policy and legal interventions

Although policy and legal interventions are not addressed as a standalone domain in the SAHCS GAHC Guideline (2021),

this rapid review identified eight studies examining the health impact of laws, regulations, and/or administrative systems on TGD youth[111,261,263,264,265,266,267,268] (Online Supplementary Appendix: Table S-L). No systematic reviews were identified.

Across both qualitative and quantitative studies, restrictive laws and systemic barriers – including outright healthcare bans, regulatory constraints, and administrative obstacles – are consistently associated with poorer mental-health outcomes, including heightened depression, anxiety, suicidality, and social isolation among TGD youth.[111,261,263,264,265,266,267,268] These associations are observed following both enacted policies and periods of policy uncertainty, suggesting that anticipatory stress and disruption to care pathways contribute to harm.

Conversely, affirming and protective policy environments, including anti-discrimination protections, inclusive institutional guidance, and accessible legal gender recognition, are associated with improved mental-health indicators and, in some analyses, lower substance use and other risk behaviours, as well as enhanced overall well-being.[261,265,267]

Parental and caregiver accounts mirror these findings, describing how proposed or enacted care bans intensified depression, anxiety, suicidality, and family distress, particularly where policies disrupted ongoing treatment or created prolonged uncertainty.[263,264,266] Across studies, families reported increased emotional burden, logistical strain, and fear related to maintaining access to care within hostile or unstable policy environments.[263,264,266]

Discussion

The global evidence base on GAHC for TGD children and adolescents has expanded rapidly since the publication of the SAHCS GAHC Guideline in 2021. Across psychosocial, endocrine, surgical, non-medical and policy interventions, the evidence from 2021 to 2025 demonstrates a consistent pattern across diverse study designs and contexts: when TGD children and adolescents receive GAHC within supportive familial, social, educational, clinical, and policy environments, outcomes are generally stable or improved, and harms are rare. Conversely, the evidence indicates that non-clinical delays in providing GAHC, as well as hostile familial, social, educational and policy environments, are associated with worsening distress and poorer mental-health outcomes. Across intervention domains, studies conducted within multidisciplinary care settings consistently report favourable safety and psychosocial outcomes, highlighting the importance of coordinated and integrated care across service levels.

Across intervention domains, the emerging evidence aligns with the 2021 SAHCS GAHC Guideline, reinforcing its core recommendations and ethical foundations, while also pointing to areas where future guideline refinements are warranted.

Strengths and limitations of this review

The review has several important strengths. It was conceived and led from South Africa by a gender and sexually diverse team with combined methodological, clinical, and lived-experience expertise. This positionality informed decisions about contextualisation and equity, ensuring that the synthesis remains grounded in the legal, social, and service realities of TGD youth in South Africa rather than importing assumptions from high-income settings. To our knowledge, this is the first comprehensive synthesis of GAHC evidence for people under 18 from the Global South.

The search strategy was broad and intentionally inclusive. We conducted a comprehensive multi-database search via EBSCOhost with no language restrictions, deliberately incorporating both current and pathologising terminology for TGD identities and interventions. Cross-mapping showed that 92 of 200 primary studies in our dataset had not appeared in any of the systematic reviews identified, substantially extending the evidence base available for synthesis and highlighting limitations in existing reviews. Data extraction and synthesis followed a structured and transparent process.

As is typical for rapid reviews, several methodological streamlining decisions were made. The review was not prospectively registered. After an initial dual-screening calibration phase, title and abstract screening proceeded with single review, with borderline or uncertain records flagged for second-reviewer input at abstract or full-text stage. Full-text screening and data extraction were not conducted in duplicate. We did not conduct a *de novo*, outcome-by-outcome risk-of-bias or GRADE/CERQual certainty assessment; instead, we drew on existing appraisals from previous systematic reviews where available and treated them as a secondary interpretive resource rather than as formal ratings for this review. No meta-analysis was attempted because of the extreme heterogeneity of designs, interventions, and outcomes. These choices are consistent with published guidance on rapid reviews, but they inevitably reduce the granularity of quality assessment and may increase susceptibility to subjective judgement compared with a fully resourced systematic review.[60,63,64,269,270]

Nonetheless, the breadth of the search, the systematic cross-linking of primary studies and prior reviews, the large number of newly identified studies, and the structured narrative synthesis conducted by a multidisciplinary author team support the robustness and practical value of the findings. The review should therefore be understood as a transparent, contextually grounded rapid synthesis rather than a definitive systematic review, and its conclusions should be interpreted with reasoned discernment and attention to the underlying evidentiary limitations.

Strengths and limitations of the evidence base covered in this review

The evidence assembled in this rapid review – spanning 200 primary studies, 29 academic systematic reviews, and four grey-literature reports – demonstrates a consistent

pattern across psychosocial, endocrine, surgical, non-medical, and policy interventions. When TGD young people access affirming psychosocial support, timely endocrine care, and, for older adolescents who require it, surgical interventions, improvements are seen in mental health, dysphoria, and day-to-day functioning. Serious adverse events are rare. Systematic reviews published since 2021, including those commissioned in politically conservative policy environments, echo these findings and report no evidence of population-level harm.[9,10,11,12,13,14,15,16,17,18,19,20,21,22,23,24,25,26,27,28,29,30,31,32,33,34,37,38,39,40,121] This consistency across diverse study designs and outcome domains strengthens confidence in the overall direction of effect, even where formal certainty ratings remain low.

Important limitations in the evidence remain. Most primary studies are observational and/or clinic-based, with small, non-representative samples, short follow-up, and limited geographic diversity. Randomised or quasi-experimental designs are scarce; they are rarely feasible or ethical in this area of care.[271] Evidence for endocrine and surgical care currently relies heavily on retrospective chart reviews, with variable data quality, inconsistent outcome recording, and limited use of patient-reported measures. Frequent access to multiple and concurrent gender-affirming intervention types by individual TGD youth constrains precision in assessing the impact of particular interventions and requires methodological advancement in the field to disentangle causality while preserving patient autonomy.

Systematic reviews reflect these constraints. Across reviews, varying assessment approaches consistently rate the certainty of evidence as low to very low, because of design limitations, small sample sizes, overlapping patient populations and interventions, short follow-up periods, and narrow geographic scope, rather than conflicting findings. These gaps underscore the need for more robust, longer-term, and inclusive research from the Global South, and South Africa in particular, to better characterise evolving health needs and support equitable, contextually responsive health-system planning.

Clinical and policy decision-making in the context of low-certainty evidence

The certainty of the evidence surrounding GAHC for youth must be understood within the broader reality that low- and very low-certainty evidence underpins a substantial proportion of medical practice overall.[272,273,274] This is particularly true in paediatrics, where ethical and logistical constraints often preclude randomised trials and contribute to persistent inconsistencies across the evidence base, even for common childhood conditions such as asthma and epilepsy.[274,275]

The recently updated GRADE Evidence-to-Decision (EtD) framework directly acknowledges these realities. As clarified in the 2025 Core GRADE 7 update,[276] low-certainty evidence typically warrants a conditional recommendation, which is an explicit signal that clinicians must engage meaningfully in shared decision-making that centres patient values and preferences. Gordon Guyatt, leading architect of the GRADE framework and co-author of systematic reviews included in this synthesis,[25,26] has explicitly cautioned against the misuse of GRADE in policy advocacy against GAHC for youth.[277] Guyatt and colleagues[277] emphasise that low-certainty evidence should not be treated as justification for withholding care, but rather as a prompt for careful clinical decision-making that centres patient values, noting:

> It is profoundly misguided to cast health care based on low-certainty evidence as bad care or as care driven by ideology, and low-certainty evidence as bad science. Many of the interventions we offer are based on low-certainty evidence […]. Thus, forbidding delivery of gender-affirming care and limiting medical management options on the basis of low-certainty evidence is a clear violation of the principles of evidence-based shared decision-making and is unconscionable.[277]

In South Africa, this is not simply a methodological consideration but a constitutional and statutory imperative. Section 129 of the *Children's Act*[278] requires respect for adolescents' evolving capacity to participate meaningfully in decisions about their own healthcare. Where the overall evidence base offers low scientific certainty yet demonstrates consistent patterns across multiple domains and outcomes, the GRADE EtD framework requires clinicians to centre patients' values, preferences, and lived experience – not to impose blanket restrictions or personal disapproval framed as clinical caution. This approach aligns with the informed-consent model endorsed in South African and international clinical guidelines on GAHC for youth.[1,8]

Implications and recommendations for South Africa

In addition to the domain-specific comparisons with the 2021 SAHCS GAHC Guideline, the evidence synthesised in this review has broader clinical and policy implications that cut across intervention areas and highlight key principles for delivering safe, effective, and contextually grounded care:

- Affirmation is central to safe and effective care, reflecting both clinical evidence and South Africa's constitutional and rights-based obligations.
- Multidisciplinary, coordinated care models that integrate medical, psychosocial, and community-based components, are associated with better outcomes across intervention domains, supporting continuity and safety of care over time.
- Structured and ongoing support for families and caregivers is essential, as affirming family environments are consistently linked with improved mental-health outcomes, sustained engagement in care, and enhanced daily functioning.
- Affirming psychosocial support should be integrated across all aspects of care, including clinical encounters, family engagement, and school or community settings, rather than treated as an ancillary component.
- Restrictive policies and administrative environments, including opaque referral structures, regulatory barriers, and medical-aid exclusions that limit

affordability, are associated with delayed or disrupted access to care and related harms.
- Supportive and protective policy environments – such as those that prohibit discrimination, provide clear clinical guidance, and support continuity of care – are associated with improved population-level well-being, including lower distress and suicidality, greater resilience, and reduced reliance on acute mental-health and emergency services.
- Health system constraints, including medication stock-outs, long waiting lists, and uneven geographic distribution of clinical expertise, require targeted policy and planning responses, as these barriers leave many adolescents without feasible routes into care.
- Equitable financing mechanisms are needed, as financial exclusion disproportionately limits access to care for economically marginalised families and entrenches inequities across provinces, and between public and private healthcare sectors.
- Strengthening adolescent-friendly services and integrated care pathways enables many non-specialised components of gender-affirming care – including psychosocial support for young people and their families, menstrual suppression, trauma-informed counselling, management of co-occurring mental-health conditions, and safe referral pathways – to be delivered within routine adolescent health and mental-health services. This approach aligns with national priorities in HIV/SRHR, youth mental health, and adolescent-friendly service delivery.
- Timely access to GAHC is a matter of health equity and cost-effective prevention, given the documented harms associated with delayed care and its downstream impacts on schooling, psychological distress, and emergency mental-health utilisation.

Priorities for future research include expanding the evidence base in low- and middle-income countries, strengthening rigour and long-term follow-up, improving the visibility of non-binary adolescents in research, investigating intersecting structural determinants of health, extending evidence on menstrual suppression and adolescent fertility pathways, and deepening TGD youths' involvement in co-produced and participatory research.

Conclusion

This rapid review provides empirical support that GAHC for TGD youth is evidence-informed, associated with improved well-being, prevents harm, and promotes healthier developmental and mental-health trajectories when delivered within supportive social, familial, clinical, and policy environments. The review affirms the evidentiary foundations of the existing South African GAHC Guideline and identifies opportunities to strengthen its implementation within South Africa's legal, historical, and health-system context. While most available studies are observational, this reflects the ethical and methodological realities of paediatric research on interventions that cannot be logistically or ethically randomised or withheld. The consistency of findings across diverse settings therefore provides compelling, real-world evidence of effectiveness and safety.

Ultimately, this work reflects South Africa's constitutional values, including dignity, equality, and the right to access healthcare without discrimination. South Africa has a long-standing tradition of protecting marginalised communities, guided by principles of collective care, justice and equity. Ensuring timely affirming care for TGD youth is both clinically sound and constitutionally grounded, representing a continuation of this legacy and a commitment to safeguarding the well-being of every young person entrusted to collective care.

Acknowledgements

The authors acknowledge Gender Dynamix for financial support, and PATHSA members for their ongoing encouragement and for modelling the collaborative spirit that anchors this work. Ariane Spitaels and Michelle Carrihill provided thoughtful input on the findings pertaining to endocrine interventions. Vanessa Mudaly assisted with abstract screening. Alasdair Allison, Rutendo Bothma and Brent Janse van Vuuren provided steady support and contributions throughout the project.

A preprint version of the full technical report was previously published on Research Square (https://doi.org/10.21203/rs.3.rs-8253372/v1), and we acknowledge its role in shaping the final article.

Artificial Intelligence Disclosure: During the preparation of this work, the authors used ChatGPT Plus (models o3 through 5.1) and Perplexity Pro to support a literature search, data extraction, and cross-check of extracted data. The content was reviewed and edited by the authors, who take full responsibility for its accuracy.

Competing interests

Ingrid Lynch, KL Dunkle, and Marion Stevens declare receiving consultancy fees for this project from Gender DynamiX. None of the other authors received remuneration for this work. Ingrid Lynch reports consultancy fees from Gender Dynamix (position paper on access to gender-affirming care), Afrikagrupperna (research on organised resistance to sexual and reproductive rights), Irise International (research on the global status of menstrual justice), and the IDRC, ICARS, and FiT-ED (gender-equity technical support). KL Dunkle declares past support from the CDC Cooperative Agreement with the SAMRC for training healthcare workers on post-violence support for LGBTQI+ survivors of violence, consulting fees from GBVF Response Fund1 (South Africa) and the Sexual Violence Research Initiative, travel support from Gender DynamiX for workshop attendance, serving as a DSMB member of Improving HIV testing, linkage, and retention in care for men through U = U messaging (1 R01 MH129223-01), and

PATHSA and WPATH membership. Chris McLachlan declares receiving honoraria from Gender DynamiX and Outright International; travel support for meetings and conferences from WPATH, PsySSA African Human Rights Project, Outright International, Gender DynamiX, SAMRC, UNISA and WHO. Chris McLachlan declares being the co-chair of WHO's Guideline Development Group, advisory board member for Wits RHI – Transgender Clinics (2022–2025), secretary of the WPATH Board, board member of PATHSA (unpaid) and executive member of PsySSA Sexuality and Gender Division. Pierre Brouard declares receiving consulting fees from Centre for Sexualities, AIDS and Gender (CSA&G), Outright International, YALI Programme, and Centre for Human Rights, UP; travel support from Gender DynamiX, Outright International, CSA&G and Centre for Human Rights, UP. Pierre Brouard also declares PATHSA board membership (unpaid), and being an executive member of the Sexuality and Gender Division, PsySSA (unpaid). Landa Mabenge declares being expert witness in the case: Mokoena v Head of Johannesburg Correctional Centre: Medium B and Others (2024/070075) [2025] ZAEQC 7 (10 Nov 2025). Sakhile Msweli declares receiving an honorarium and travel support for training from Gender DynamiX, PsySSA African Human rights Project and SAMRC, and being a board member of PATHSA (unpaid). Liberty Matthyse declares that she is the executive director of Gender DynamiX, and board member of the International Trans Fund, and declares funding from the Co-Impact Gender Fund for just health systems strengthening work with Gender Dynamix. Marion Stevens declares receiving consultancy fees from Gender DynamiX, Triangle Project, SAMRC and the PEARLs study for Pre-Eclampsia at the Department of Gynaecology, University of Cape Town. Marion Stevens further declares having been a Consolidoc Fellow (Nov 2024 – Feb 2025), Department of Political Sciences, Stellenbosch University, and travel support to attend the 30th year anniversary of the Commission on Gender Equality and for meetings of the Gender Advisory Panel of the WHO (term completed 2024). Robin Dyers declares an NIHR Grant for research: PCAT in Southern Africa, receiving an honorarium and travel support for training from Gender DynamiX, travel support from Taiwan ICDF and WHO, being treasurer of the PATHSA board (unpaid), member of WHO FIC CC South Africa – MRCSA (unpaid) and board member of Project Flamingo (unpaid). Jenna-Lee de Beer-Procter declares being vice chair of the PATHSA board (unpaid), and co-chair of the WPATH International Outreach Committee (unpaid). Kevin Adams declares PATHSA board membership (unpaid). W.D. Francois Venter declares that his unit receives funding from the Bill and Melinda Gates Foundation, SAMRC, NIH, Unitaid, Foundation for Innovative New Diagnostics (FIND), Merck and the Children's Investment Fund Foundation (CIFF), has previously received funding from USAID, and received drug donations from ViiV Healthcare, Merck, J&J and Gilead Sciences for investigator-led clinical studies. The unit does investigator-led studies with Merck, J&J, Gilead, and ViiV providing financial support and is doing commercial drug studies for Merck and Novo. The unit performs evaluations of diagnostic devices for multiple biotech companies. W.D. Francois Venter receives honoraria for educational talks and advisory board membership for Gilead, ViiV, Mylan/Viatris, Merck, Adcock-Ingram, Aspen, Abbott, Roche, J&J, Sanofi, Boehringer Ingelheim, Thermo-Fischer, and Virology Education. W.D. Francois Venter serves on the NIH International DSMB, and the board of Dira Sengwe (unpaid). Elma de Vries declares receiving an honorarium and travel support for training from Gender DynamiX, travel support from WHO for a Guideline Development Group Meeting in August 2024, serving as a member of the Wits RHI Technical Advisory Group–Transgender clinics (2022–2025), being board chairperson of PATHSA (unpaid), and a member of WPATH.

CRediT authorship contribution

Ingrid Lynch: Data curation, Formal analysis, Investigation, Methodology, Validation, Writing – original draft, Writing – review & editing. KL Dunkle: Conceptualisation, Data curation, Formal analysis, Investigation, Methodology, Software, Validation, Writing – original draft, Writing – review & editing. Chris McLachlan: Conceptualisation, Writing – original draft, Writing – review & editing. Pierre Brouard: Conceptualisation, Writing – original draft, Writing – review & editing. Landa Mabenge: Writing – original draft, Writing – review & editing. Sakhile Msweli: Conceptualisation, Writing – original draft, Writing – review & editing. Liberty Matthyse: Conceptualisation, Funding acquisition, Writing – review & editing. Marion Stevens: Writing – original draft, Writing – review & editing. Robin Dyers: Conceptualisation, Data curation, Writing – review & editing. Jenna-Lee de Beer-Procter: Conceptualisation, Writing – original draft, Writing – review & editing. Kevin Adams: Writing – review & editing. W.D. Francois Venter: Conceptualisation, Writing – original draft, Writing – review & editing. Elma de Vries: Conceptualisation, Data curation, Writing – original draft, Writing – review & editing. All authors reviewed the article, contributed to the discussion of results, approved the final version for submission and publication, and take responsibility for the integrity of its findings.

Ethical considerations

This article followed all ethical standards for research without direct contact with human or animal subjects.

Funding information

Ingrid Lynch, KL Dunkle, and Marion Stevens declare receiving consultancy fees for this project from Gender DynamiX. None of the other authors received remuneration for this work.

Data availability

The authors confirm that the data supporting the findings of this study are available within the article and its references, and in the Online Supplementary Appendix file published with this article.

Disclaimer

The views and opinions expressed in this article are those of the authors and are the product of professional research. They do not necessarily reflect the official policy or position of any affiliated institution, funder, agency, or that of the publisher. The authors are responsible for this article's results, findings, and content.

References

1. Coleman E, Radix AE, Bouman WP, et al. Standards of care for the health of transgender and gender diverse people, version 8. Int J Transgender Health. 2022;23(Suppl 1):S1–S259. https://doi.org/10.1080/26895269.2022.2100644
2. Budge SL, Abreu RL, Flinn RE, et al. Gender affirming care is evidence based for transgender and gender-diverse youth. J Adolesc Health. 2024;75(6):851–853. https://doi.org/10.1016/j.jadohealth.2024.09.009
3. Cloete A, Mabaso M, Savva H, et al. The HIV care continuum for sexually active transgender women in three metropolitan municipalities in South Africa: Findings from a biobehavioural survey 2018–19. Lancet HIV. 2023;10(6): e375–e384. https://doi.org/10.1016/S2352-3018(23)00059-0
4. Shabalala SB, Campbell MM. The complexities of trans women's access to healthcare in South Africa: Moving health systems beyond the gender binary towards equity. Int J Equity Health. 2023;22(231):1–12. https://doi.org/10.21203/rs.3.rs-3237907/v1
5. Zambezi D, Viljoen F. Access to healthcare services for transgender people in South Africa: Assessing healthcare experiences and human rights. Int J Transgender Health. 2024;25(4):791–803. https://doi.org/10.1080/26895269.2023.2273364
6. Bothma R, O'Connor C, Nkusi J, et al. Differentiated HIV services for transgender people in four South African districts: Population characteristics and HIV care cascade. J Int AIDS Soc. 2022;25(S5):e25987. https://doi.org/10.1002/jia2.25987
7. National Department of Health. The national strategic plan for HIV, TB, and STIs 2023–2028 [homepage on the Internet]. c2023 [cited 2025 Sep 29]. Available from: https://knowledgehub.health.gov.za/elibrary/national-strategic-plan-hiv-tb-and-stis-2023-2028
8. Tomson A, McLachlan C, Wattrus C, et al. Southern African HIV Clinicians' Society gender-affirming healthcare guideline for South Africa – Expanded version [homepage on the Internet]. c2021 [cited 2025 Sep 29]. Available from: https://sahivsoc.org/Subheader/Index/sahcs-guidelines
9. Baker KE, Wilson LM, Sharma R, Dukhanin V, McArthur K, Robinson KA. Hormone therapy, mental health, and quality of life among transgender people: A systematic review. J Endocr Soc. 2021;5(4):bvab011. https://doi.org/10.1210/jendso/bvab011
10. Chesters M, Pipkin A, Brett CE. A systematic review of interventions with families of trans people. Int J Transgender Health. 2025:1–19. https://doi.org/10.1080/26895269.2025.2492614
11. Christensen JA, Oh J, Linder K, et al. Systematic review of interventions to reduce suicide risk in transgender and gender diverse youth. Child Psychiatry Hum Dev. 2025;56(1):88–100. https://doi.org/10.1007/s10578-023-01541-w
12. D'hoore L, T'Sjoen G. Gender-affirming hormone therapy: An updated literature review with an eye on the future. J Intern Med. 2022;291(5):574–592. https://doi.org/10.1111/joim.13441
13. Day M, Brömdal A. Mental health outcomes of transgender and gender diverse students in schools: A systematic literature review. Int J Transgender Health. 2024;27(1):1–21. https://doi.org/10.1080/26895269.2024.2359934
14. Diana P, Belluzzi B, Corona F, Barbi E, Tornese G. Nonmedical gender-affirming practices in transgender and gender diverse adolescents: A narrative review. Transgender Health. 2024;11(2):1–8. https://doi.org/10.1089/trgh.2023.0194
15. Expósito-Campos P, Pérez-Fernández JI, Salaberria K. Empirically supported affirmative psychological interventions for transgender and non-binary youth and adults: A systematic review. Clin Psychol Rev. 2023;100:102229. https://doi.org/10.1016/j.cpr.2022.102229
16. Feigerlova E. Prevalence of detransition in persons seeking gender-affirming hormonal treatments: A systematic review. J Sex Med. 2025;22(2):356–368. https://doi.org/10.1093/jsxmed/qdae186
17. Goulding R, Goodwin J, O'Donovan A, Saab MM. Transgender and gender diverse youths' experiences of healthcare: A systematic review of qualitative studies. J Child Health Care. 2025;29(2):523–545. https://doi.org/10.1177/13674935231222054
18. Gupta P, Cunha LM, Diego D, Tangpricha V. Continuation of gender-affirming hormone therapy in transgender and gender-diverse individuals: A systematic review. Endocr Pract. 2024;30(12):1206–1211. https://doi.org/10.1016/j.eprac.2024.09.007
19. Hall R, Taylor J, Hewitt CE, et al. Impact of social transition in relation to gender for children and adolescents: A systematic review. Arch Dis Child. 2024;109(Suppl 2):s12–s18. https://doi.org/10.1136/archdischild-2023-326112
20. Heathcote C, Taylor J, Hall R, et al. Psychosocial support interventions for children and adolescents experiencing gender dysphoria or incongruence: A systematic review. Arch Dis Child. 2024;109(Suppl 2):s19–s32. https://doi.org/10.1136/archdischild-2023-326347
21. Ludvigsson JF, Adolfsson J, Höistad M, Rydelius PA, Kriström B, Landén M. A systematic review of hormone treatment for children with gender dysphoria and recommendations for research. Acta Paediatr Oslo Nor 1992. 2023;112(11):2279–2292. https://doi.org/10.1111/apa.16791
22. Malpas J, Pellicane MJ, Glaeser E. Family-based interventions with transgender and gender expansive youth: Systematic review and best practice recommendations. Transgender Health. 2022;7(1):7–29. https://doi.org/10.1089/trgh.2020.0165
23. Manley J, Brownlow C, Brömdal A. Supporting the health and wellbeing of trans autistic school-aged youth: A systematic literature review. Int J Transgender Health. 2024;25(3):439–455. https://doi.org/10.1080/26895269.2024.2317392
24. Mezzalira S, Scandurra C, Mezza F, Miscioscia M, Innamorati M, Bochicchio V. Gender felt pressure, affective domains, and mental health outcomes among transgender and gender diverse (TGD) children and adolescents: A systematic review with developmental and clinical implications. Int J Environ Res Public Health. 2022;20(1):785. https://doi.org/10.3390/ijerph20010785
25. Miroshnychenko A, Ibrahim S, Roldan Y, et al. Gender affirming hormone therapy for individuals with gender dysphoria aged <26 years: A systematic review and meta-analysis. Arch Dis Child. 2025;110(6):437–445. https://doi.org/10.1136/archdischild-2024-327921
26. Miroshnychenko A, Roldan Y, Ibrahim S, et al. Puberty blockers for gender dysphoria in youth: A systematic review and meta-analysis. Arch Dis Child. 2025;110(6):429–436. https://doi.org/10.1136/archdischild-2024-327909
27. Ramos GGF, Mengai ACS, Daltro CAT, Cutrim PT, Zlotnik E, Beck APA. Systematic review: Puberty suppression with GnRH analogues in adolescents with gender incongruity. J Endocrinol Invest. 2021;44(6):1151–1158. https://doi.org/10.1007/s40618-020-01449-5
28. Rew L, Young CC, Monge M, Bogucka R. Review: Puberty blockers for transgender and gender diverse youth – A critical review of the literature. Child Adolesc Ment Health. 2021;26(1):3–14. https://doi.org/10.1111/camh.12437
29. Sánchez-Reyes L, Anguita-Martínez R, Castro-Alija MJ. Mental health and health care for transgender and gender nonconforming adolescents: A systematic review. Pap Psicól. 2024;45(3):136–145. https://doi.org/10.23923/pap.psicol.3042
30. Stolk THR, Asseler JD, Huirne JAF, Van den Boogaard E, Van Mello NM. Desire for children and fertility preservation in transgender and gender-diverse people: A systematic review. Best Pract Res Clin Obstet Gynaecol. 2023;87:102312. https://doi.org/10.1016/j.bpobgyn.2023.102312
31. Tankersley AP, Grafsky EL, Dike J, Jones RT. Risk and resilience factors for mental health among transgender and gender nonconforming (TGNC) youth: A systematic review. Clin Child Fam Psychol Rev. 2021;24(2):183–206. https://doi.org/10.1007/s10567-021-00344-6
32. Taylor J, Mitchell A, Hall R, Langton T, Fraser L, Hewitt CE. Masculinising and feminising hormone interventions for adolescents experiencing gender dysphoria or incongruence: A systematic review. Arch Dis Child. 2024;109(Suppl 2):s48–s56. https://doi.org/10.1136/archdischild-2023-326670
33. Taylor J, Mitchell A, Hall R, et al. Interventions to suppress puberty in adolescents experiencing gender dysphoria or incongruence: A systematic review. Arch Dis Child. 2024;109(Suppl 2):s33–s47. https://doi.org/10.1136/archdischild-2023-326669
34. Thompson L, Sarovic D, Wilson P, et al. A PRISMA systematic review of adolescent gender dysphoria literature: 3) treatment. PLOS Glob Public Health. 2023;3(8):e0001478. https://doi.org/10.1371/journal.pgph.0001478
35. Tornese G, Di Mase R, Munarin J, et al. Use of gonadotropin-releasing hormone agonists in transgender and gender diverse youth: A systematic review. Front Endocrinol. 2025;16:1555186. https://doi.org/10.3389/fendo.2025.1555186
36. Tyler TR, Huddleston BS, Kronner HW, et al. Qualitative metasummary: Transgender and gender diverse children's experiences of parental responses. LGBTQ Fam Interdiscip J. 2024;20(5):394–416. https://doi.org/10.1080/27703371.2024.2346556
37. Bragge P, Cong-Lem N, Delafosse V, Goldberg E, Temple-Smith M, Sanci L. Evidence check: Evidence for effective interventions for children and young people with gender dysphoria—update: An Evidence Check rapid review brokered by the Sax Institute for the NSW Ministry of Health. Sydney: Sax Institute; 2024.
38. Dopp AR, Peipert A, Buss J, De Jesús-Romero R, Palmer K, Lorenzo-Luaces L. Interventions for gender dysphoria and related health problems in transgender and gender-expansive youth: A systematic review of benefits and risks to inform practice, policy, and research. Santa Monica, CA: RAND Corporation; 2024.
39. Ministry of Health. Impact of puberty blockers in gender-dysphoric adolescents: An evidence brief. Wellington: Ministry of Health, New Zealand; 2024.
40. LaFleur L, Heath L, Gonzales V, et al. Gender-affirming medical treatments for pediatric patients with gender dysphoria [homepage on the Internet]. c2024 [cited 2025 Aug 14]. Available from: https://www.researchgate.net/publication/400035576_Gender-affirming_medical_treatments_for_pediatric_patients_with_gender_dysphoria
41. Brezin F, Busiah K, Leroy C, et al. Endocrine management of transgender adolescents: Expert consensus of the French Society of Pediatric Endocrinology and Diabetology Working Group. Arch Pediatr. 2024. https://doi.org/10.1016/j.arcped.2024.08.003
42. Telfer MM, Tollit MA, Pace CC, Pang KC. Australian Standards of Care and Treatment Guidelines for Trans and Gender Diverse Children and Adolescents Version 1.4. [homepage on the Internet]. Melbourne: The Royal Children's Hospital; 2023 [cited 2025 Sep 29]. Available from: https://www.rch.org.au/uploadedFiles/Main/Content/adolescent-medicine/230242%20RCH%20Gender%20Standards%20Booklet%201.4_Nov%202023_WEB.pdf
43. Gawlik-Starzyk A, Dora M, Baran D, et al. Framework guidelines for the process of caring for the health of adolescent transgender (T) and non-binary (NB) people experiencing gender dysphoria – The position statement of the expert panel. Endokrynol Pol. 2025;76(1):1–28. https://doi.org/10.5603/ep.104289

44. 性別不合に関する診断と治療のガイドライン（第5版） [Guidelines for the diagnosis and treatment of gender incongruence]. Jpn Soc Psychiatry Neurol [serial online]. c2024 [cited 2025 Sep 29]. Available from: https://www.jspn.or.jp/uploads/uploads/files/activity/gid_guideline_no5.pdf

45. German Society for Child and Adolescent Psychiatry, Psychosomatics and Psychotherapy (DGKJP), et al. Geschlechtsinkongruenz und Geschlechtsdysphorie im Kindes- und Jugendalter – Diagnostik und Behandlung (S2k-Leitlinie), AWMF-Registernr. 028-014 [Gender incongruence and gender dysphoria in childhood and adolescence – diagnosis and treatment]. Berlin: AWMF; 2025 [cited 2025 Sep 29]. Available from: https://register.awmf.org/de/leitlinien/detail/028-014

46. Matthyse L, Payne AL, Mudarikwa M, Smit E, Camminga B, Rossouw R. Keeping the promise of dignity and freedom for all: A position paper on legal gender recognition in South Africa [homepage on the Internet]. c2020 [cited 2025 Sep 29]. Available from: https://www.genderdynamix.org.za/_files/ugd/3486ef_bf9c6bdb89184295b9910d25b7296561.pdf?index=true

47. Ozah K. Informed consent and access to gender-affirming treatment for children in South Africa. Jure. 2023;56(1):569–587. https://doi.org/10.17159/2225-7160/2023/v56a34

48. Republic of South Africa. The Constitution of the Republic of South Africa [homepage on the Internet]. c1996 [cited 2025 Sep 29]. Available from: https://www.justice.gov.za/constitution/SAConstitution-web-eng.pdf

49. Boulware S, Kamody R, Kuper L, et al. Biased science: The Texas and Alabama measures criminalizing medical treatment for transgender children and adolescents rely on inaccurate and misleading scientific claims. SSRN Electron J. 2022. https://doi.org/10.2139/ssrn.4102374

50. Horton C. The Cass Review: Cis-supremacy in the UK's approach to healthcare for trans children. Int J Transgender Health. 2024;26(4):1120–1144. https://doi.org/10.1080/26895269.2024.2328249

51. Hughes LD, Kidd KM, Gamarel KE, Operario D, Dowshen N. 'These laws will be devastating': Provider perspectives on legislation banning gender-affirming care for transgender adolescents. J Adolesc Health. 2021;69(6):976–982. https://doi.org/10.1016/j.jadohealth.2021.08.020

52. Human Rights Watch. 'They're ruining people's lives': Bans on gender-affirming care for transgender youth in the US [homepage on the Internet]. c2025 [cited 2025 Sep 29]. Available from: https://www.hrw.org/sites/default/files/media_2025/05/lgbt_us0625web.pdf

53. Wuest J, Last BS. Agents of scientific uncertainty: Conflicts over evidence and expertise in gender-affirming care bans for minors. Soc Sci Med 1982. 2024;344:116533. https://doi.org/10.1016/j.socscimed.2023.116533

54. Gouws A, Zyl MV. Towards a feminist ethics of ubuntu: Bridging rights and ubuntu. In: Engster D, Hamington M, editors. Care ethics and political theory [homepage on the Internet]. Oxford: Oxford University Press, 2015 [cited 2025 Dec 18]; p. 164–186. Available from: https://academic.oup.com/book/1506/chapter/140936023.

55. Nicolaides A. Considering the philosophy of Ubuntu in South African healthcare ethical practices. J Med Lab Sci Technol South Afr. 2023;5(1):71–76. https://doi.org/10.36303/JMLSTSA.133

56. Republic of South Africa. White paper on transforming public service delivery (Batho Pele White Paper). Report 1459 of 1997. Pretoria: Department of Public Service and Administration; 1997 [cited n.d.]. Available from: https://www.dpsa.gov.za/dpsa2g/documents/acts&regulations/frameworks/white-papers/transpubservice.pdf

57. Bust L, Matyila SA, Welte O, et al. Gender-affirming care in South Africa: A cross-sectional survey of transgender and gender-diverse people in the Eastern and Western Cape provinces, South Africa. S Afr Med J. 2026;116(1):e3253. https://doi.org/10.7196/SAMJ.2026.v116i1.3523

58. Mahlobogwane F. Barriers to gender-affirming health care in children and adolescents in South Africa. Obiter. 2025;46(2):312–327. https://doi.org/10.17159/k75sqa82

59. Ritshidze. State of healthcare for key populations [homepage on the Internet]. c2024 [cited 2025 Dec 07]. Available from: https://ritshidze.org.za/wp-content/uploads/2024/02/Ritshidze-State-of-Healthcare-for-Key-Populations-2024.pdf

60. Garritty C, Tricco AC, Smith M, et al. Rapid reviews methods series: Involving patient and public partners, healthcare providers and policymakers as knowledge users. BMJ Evid Based Med. 2024;29(1):55–61. https://doi.org/10.1136/bmjebm-2022-112070

61. Bothma R, Pettifor A, Maphosa I, Ndlovu P, Imrie J, Poteat T. Exploring healthcare experiences of transgender people in the Jabula Uzibone study, South Africa: A longitudinal implementation science study. J Int AIDS Soc. 2025;28(Suppl 3):e26503. https://doi.org/10.1002/jia2.26503

62. Naledi T, Stevens M, De Vries E. When we know better, we must do better: Gender affirming healthcare as a test of justice. Int J Transgender Health. 2026;27(3):1173–1177. https://doi.org/10.1080/26895269.2025.2549122

63. Devane D, Hamel C, Gartlehner G, et al. Key concepts in rapid reviews: An overview. J Clin Epidemiol. 2024;175:111518. https://doi.org/10.1016/j.jclinepi.2024.111518

64. Stevens A, Garritty C, Hersi M, Moher D. Developing PRISMA-RR, a reporting guideline for rapid reviews of primary studies (Protocol) [homepage on the Internet]. c2018 [cited 2025 Nov 25]. Available from: https://www.equator-network.org/wp-content/uploads/2018/02/PRISMA-RR-protocol.pdf

65. McKenzie JE, Brennan SE, Ryan RE, Thomson HJ, Johnston RV, Thomas J. Defining the criteria for including studies and how they will be grouped for the synthesis. In: Higgins JPT, Thomas J, Chandler J, editors. Cochrane handbook for systematic reviews of interventions [homepage on the Internet]. Cochrane; c2019 [cited 2025 Nov 25]. Available from: https://www.cochrane.org/authors/handbooks-and-manuals/handbook/current/chapter-03

66. Page MJ, McKenzie JE, Bossuyt PM, et al. The PRISMA 2020 statement: An updated guideline for reporting systematic reviews. Syst Rev. 2021;10(1):89. https://doi.org/10.1186/s13643-021-01626-4

67. Haddaway NR, Page MJ, Pritchard CC, McGuinness LA. PRISMA 2020: An R package and Shiny app for producing PRISMA 2020-compliant flow diagrams, with interactivity for optimised digital transparency and open synthesis. Campbell Syst Rev. 2022;18(2):e1230. https://doi.org/10.1002/cl2.1230

68. Allen SD, Tollit MA, McDougall R, Eade D, Hoq M, Pang KC. A waitlist intervention for transgender young people and psychosocial outcomes. Pediatrics. 2021;148(2):e2020042762. https://doi.org/10.1542/peds.2020-042762

69. Amos N, Grant R, Lin A, et al. Mental health and wellbeing outcomes among trans young people in Australia who are supported to affirm their gender. J Adolesc Health. 2025;77(1):51–58. https://doi.org/10.1016/j.jadohealth.2025.03.011

70. Barras A, Jones BA. '[He] can be supportive, but at times I feel he is ashamed of me': Understanding the relationship between parental support and quality of life amongst trans and gender diverse youth in the UK. Int J Transgender Health. 2024;25(1):90–101. https://doi.org/10.1080/26895269.2023.2286269

71. Bauermeister J, Choi SK, Bruehlman-Senecal E, et al. An identity-affirming web application to help sexual and gender minority youth cope with minority stress: Pilot randomized controlled trial. J Med Internet Res. 2022;24(8):e39094. https://doi.org/10.2196/39094

72. Belmont N, Cronin TJ, Pepping CA. Affirmation-support, parental conflict, and mental health outcomes of transgender and gender diverse youth. Int J Transgender Health. 2023;25(1):50–62. https://doi.org/10.1080/26895269.2023.2252418

73. Bluth K, Lathren C, Clepper-Faith M, Larson LM, Ogunbamowo DO, Pflum S. Improving mental health among transgender adolescents: Implementing mindful self-compassion for teens. J Adolesc Res. 2023;38(2):271–302. https://doi.org/10.1177/07435584211062126

74. Bluth K, Bryce A, Lathren CR, Park J, Pflum S, Clayton M. Reducing suicide ideation in transgender adolescents with mindful self-compassion: An open trial. Mindfulness. 2024;15(12):3107–3128. https://doi.org/10.1007/s12671-024-02421-7

75. Brandsma T, Visser K, Volk JJG, Van Rijn AB, Dekker LP. A pilot study on the effect of peer support on quality of life of adolescents with autism spectrum disorder and gender dysphoria. J Autism Dev Disord. 2024;54(3):997–1008. https://doi.org/10.1007/s10803-022-05832-4

76. Campbell T, Mann S, Van der Meulen Rodgers Y, Tran NM. Mental health of transgender youth following gender identity milestones by level of family support. JAMA Pediatr. 2024;178(9):870–878. https://doi.org/10.1001/jamapediatrics.2024.2035

77. Campbell T, Van der Meulen Rodgers Y. Conversion therapy, suicidality, and running away: An analysis of transgender youth in the U.S. J Health Econ. 2023;89:102750. https://doi.org/10.1016/j.jhealeco.2023.102750

78. Cavve BS, Bickendorf X, Ball J, et al. Reidentification with birth-registered sex in a western Australian pediatric gender clinic cohort. JAMA Pediatr. 2024;178(5):446–453. https://doi.org/10.1001/jamapediatrics.2024.0077

79. Chinsen A, Tollit MA, Heye PL, Pang KC, Cronin TJ, Pace CC. 'I could be one of those people that's alive and happy': A qualitative exploration of a co-designed group therapy program targeting gender minority stress for trans young people (TAG TEAM). Int J Transgender Health. 2026;27(3):1359–1375. https://doi.org/10.1080/15532739.2025.2472950

80. De Castro Peraza ME, Lorenzo Rocha ND, García Acosta JM, et al. Beneficios de la transición social temprana en menores transgénero. Perspectivas de familias: estudio cualitativo [Benefits of early social transition in transgender minors. Family perspectives: Qualitative study]. Rev Esp Salud Publica. 2023;97:e202301007.

81. Durwood L, Eisner L, Fladeboe K, et al. Social support and internalizing psychopathology in transgender youth. J Youth Adolesc. 2021;50(5):841–854. https://doi.org/10.1007/s10964-020-01391-y

82. Durwood L, Kuvalanka KA, Kahn-Samuelson S, et al. Retransitioning: The experiences of youth who socially transition genders more than once. Int J Transgender Health. 2022;23(4):409–427. https://doi.org/10.1080/26895269.2022.2085224

83. Durwood L, Gallagher NM, Sifre R, Olson KR. A study of parent-reported internalizing symptoms in transgender youth before and after childhood social transitions. Clin Psychol Sci. 2024;12(5):984–996. https://doi.org/10.1177/21677026231208086

84. Esposito EC, Ellerkamp H, Eisenberg AM, Handley ED, Glenn CR. Suicide ideation among transgender and gender diverse adolescents: The role of parental invalidation of adolescents' gender identity. Res Child Adolesc Psychopathol. 2024;52(9):1329–1342. https://doi.org/10.1007/s10802-024-01203-y

85. Gadomski AM, Scribani MB, Tallman N, O'Bryan J, Wolf-Gould C, Wolf-Gould C. Two-year follow-up study of health-related quality of life among transgender and gender expansive youth receiving gender-affirming care. Transgender Health. 2024;9(5):389–398. https://doi.org/10.1089/trgh.2022.0165

86. Garrick C, Bear B, Gannon M, et al. Social support related to menses in gender-diverse adolescents: A qualitative study. J Pediatr Adolesc Gynecol. 2025;38(5):585–591. https://doi.org/10.1016/j.jpag.2025.04.006

87. Gelly MA, Atgé-Delbays S, Gravel É, Sansfaçon AP. Gender-related medical experiences of youth who have detranstioned. J Homosex. 2025;72(6):1002–1024. https://doi.org/10.1080/00918369.2024.2362268

88. Gelly MA, Atgé-Delbays S, Sansfaçon AP. 'They're unable to see my decision to detransition for what it is': How detrans youth perceive and receive discourses on detransition. Sex Res Soc Policy. 2025;22:1748–1764. https://doi.org/10.1007/s13178-024-01079-z

89. Gibson DJ, Glazier JJ, Olson KR. Evaluation of anxiety and depression in a community sample of transgender youth. JAMA Netw Open. 2021;4(4):e214739. https://doi.org/10.1001/jamanetworkopen.2021.4739

90. González-Mendiondo L, Moyano N, Mayor A. 'I don't want to be a girl. I am a girl!' experiences before, during and after transition in families with trans children and adolescents. J Child Fam Stud. 2024;33(6):1695–1711. https://doi.org/10.1007/s10826-024-02832-z

91. Grant R, Amos N, Lin A, et al. Mental health and wellbeing outcomes associated with social, medical, and legal gender affirmation among trans young people in Australia. Int J Transgender Health. 2024;27(1):289–301. https://doi.org/10.1080/26895269.2024.2366881

92. Grossman AH, Park JY, Frank JA, Russell ST. Parental responses to transgender and gender nonconforming youth: Associations with parent support, parental abuse, and youths' psychological adjustment. J Homosex. 2021;68(8):1260–1277. https://doi.org/10.1080/00918369.2019.1696103

93. Horton C. 'Euphoria': Trans children and experiences of prepubertal social transition. Fam Relat. 2022;72(4):1890–1907. https://doi.org/10.1111/fare.12764

94. Horton C. 'I was losing that sense of her being happy': Trans children and delaying social transition. LGBTQ Fam Interdiscip J. 2022;18(2):187–203. https://doi.org/10.1080/27703371.2022.2076002

95. Horton C. Gender minority stress in education: Protecting trans children's mental health in UK schools. Int J Transgender Health. 2023;24(2):195–211. https://doi.org/10.1080/26895269.2022.2081645

96. Kennedy KS, Harper CR, Li J, Suarez NA, Johns MM. Protective environments, health, and substance use among transgender and gender expansive youth. LGBT Health. 2022;9(6):393–400. https://doi.org/10.1089/lgbt.2021.0258

97. Kirchner S, Till B, Plöderl M, Niederkrotenthaler T. Effects of 'It Gets Better' suicide prevention videos on youth identifying as lesbian, gay, bisexual, transgender, queer, or other sexual or gender minorities: A randomized controlled trial. LGBT Health. 2022;9(6):436–446. https://doi.org/10.1089/lgbt.2021.0383

98. Lim G, Buckingham P, McGowan I, et al. Exploring trans youths' future orientations as a product of experiences of dis/affirmation. J Sociol. 2025;61(3):547–568. https://doi.org/10.1177/14407833251314008

99. Lucassen MFG, Stasiak K, Fleming T, et al. Computerized cognitive behavioural therapy for gender minority adolescents: Analysis of the real-world implementation of SPARX in New Zealand. Aust N Z J Psychiatry. 2021;55(9):874–882. https://doi.org/10.1177/0004867420976846

100. Mackie G, Patlamazoglou L, Lambert K. The experiences of Australian transgender young people in school counseling: An interpretative phenomenological analysis. Psychol Sex Orientat Gend Divers. 2023;10(2):337–349. https://doi.org/10.1037/sgd0000544

101. McGregor K, Rana V, McKenna JL, Williams CR, Vu A, Boskey ER. Understanding family support for transgender youth: Impact of support on psychosocial functioning. J Adolesc Health. 2024;75(2):261–266. https://doi.org/10.1016/j.jadohealth.2024.04.006

102. Miller GH, Marquez-Velarde G, Suárez MI, Glass C. Support saves lives: Exploring the relationship between age of transition, family support, and retrospective K-12 educational experiences in transgender suicidality. Transgender Health. 2024;9(2):118–127. https://doi.org/10.1089/trgh.2022.0073

103. Morandini JS, Kelly A, De Graaf NM, et al. Is social gender transition associated with mental health status in children and adolescents with gender dysphoria? Arch Sex Behav. 2023;52(3):1045–1060. https://doi.org/10.1007/s10508-023-02588-5

104. Nath R, Hobaica S, DeChants JP. The relationship between parental and caregiver support and suicide among LGBTQ+ youth of color. J Adolesc Health. 2025;76(4):606–612. https://doi.org/10.1016/j.jadohealth.2024.11.242

105. Oliver M, Poysden Z, Crowe E, et al. 'Just listen to me. Help me explore it'. An interpretative phenomenological analysis exploring experiences of gender dysphoria, identity and resilience in autistic adolescents assigned female at birth. J Autism Dev Disord. 2026(56):1934–1951. https://doi.org/10.1007/s10803-024-06688-6

106. Olsavsky AL, Grannis C, Bricker J, et al. Associations among gender-affirming hormonal interventions, social support, and transgender adolescents' mental health. J Adolesc Health. 2023;72(6):860–868. https://doi.org/10.1016/j.jadohealth.2023.01.031

107. Olson KR, Durwood L, Horton R, Gallagher NM, Devor A. Gender identity 5 years after social transition. Pediatrics. 2022;150(2):e2021056082. https://doi.org/10.1542/peds.2021-056082

108. Parodi KB, Holt MK, Green JG, et al. Associations between school-related factors and mental health among transgender and gender diverse youth. J Sch Psychol. 2022;90:135–149. https://doi.org/10.1016/j.jsp.2021.11.004

109. Price MN, Green AE. Association of gender identity acceptance with fewer suicide attempts among transgender and nonbinary youth. Transgender Health. 2023;8(1):56–63. https://doi.org/10.1089/trgh.2021.0079

110. Pullen Sansfaçon A, Medico D, Gelly M, Kirichenko V, Suerich-Gulick F, on behalf of the Stories of Gender Affirming Care Project. Blossoming child, mourning parent: A qualitative study of trans children and their parents navigating transition. J Child Fam Stud. 2022;31(7):1771–1784. https://doi.org/10.1007/s10826-021-02178-w

111. Pullen Sansfaçon A, Medico D, Riggs D, Carlile A, Suerich-Gulick F. Growing up trans in Canada, Switzerland, England, and Australia: Access to and impacts of gender-affirming medical care. J LGBT Youth. 2023;20(1):55–73. https://doi.org/10.1080/19361653.2021.1924918

112. Sievert EDC, Schweizer K, Barkmann C, Fahrenkrug S, Becker-Hebly I. Not social transition status, but peer relations and family functioning predict psychological functioning in a German clinical sample of children with Gender Dysphoria. Clin Child Psychol Psychiatry. 2021;26(1):79–95. https://doi.org/10.1177/1359104520964530

113. Skelton S, Riggs DW, Pullen Sansfacon A, Katz-Wise SL, Arora M, Thibeault CA. 'It just feels really nice when people call me by my name': Accounts of gender euphoria among Australian trans young people and their parents. J Gend Stud. 2024;33(4):470–482. https://doi.org/10.1080/09589236.2023.2285984

114. Strang JF, Knauss M, Van der Miesen A, et al. A clinical program for transgender and gender-diverse neurodiverse/autistic adolescents developed through community-based participatory design. J Clin Child Adolesc Psychol. 2021;50(6):730–745. https://doi.org/10.1080/15374416.2020.1731817

115. Thoma BC, Jardas EJ, Choukas-Bradley S, Salk RH. Perceived gender transition progress, gender congruence, and mental health symptoms among transgender adolescents. J Adolesc Health. 2023;72(3):444–451. https://doi.org/10.1016/j.jadohealth.2022.09.032

116. Toomey RB, Trujillo L, Abreu RL, Rios Garza A, Hainsworth S, Zhao Z. The potential harm of loss and grief narratives among families of transgender and nonbinary youth. J Couns Psychol. 2025;72(3):201–210. https://doi.org/10.1037/cou0000778

117. Turban JL, King D, Li JJ, Keuroghlian AS. Timing of social transition for transgender and gender diverse youth, K-12 harassment, and adult mental health outcomes. J Adolesc Health. 2021;69(6):991–998. https://doi.org/10.1016/j.jadohealth.2021.06.001

118. Tyni K, Wurm M, Sofia Bratt A. A thematic analysis of the experiences of prepubertal transgender and gender-diverse children in Sweden. Int J LGBTQ Youth Stud. 2025;22(3):466–489. https://doi.org/10.1080/19361653.2024.2347957

119. Van der Vaart LR, Verveen A, Bos HM, Van Rooij FB, Steensma TD. Differences in self-perception and social gender status in children with gender incongruence. Clin Child Psychol Psychiatry. 2022;27(4):1077–1090. https://doi.org/10.1177/13591045221099394

120. Weinhardt LS, Wesp LM, Xie H, et al. Pride Camp: Pilot study of an intervention to develop resilience and self-esteem among LGBTQ youth. Int J Equity Health. 2021;20(1):150. https://doi.org/10.1186/s12939-021-01488-1

121. Xu L, Roegman R. Protective factors for transgender and gender non-conforming youth's high school experience: A systematic literature review. Int J LGBTQ Youth Stud. 2025;22(1):106–125. https://doi.org/10.1080/19361653.2023.2286226

122. McGregor K, McKenna JL, Williams CR, Barrera EP, Boskey ER. Association of pubertal blockade at Tanner 2/3 with psychosocial benefits in transgender and gender diverse youth at hormone readiness assessment. J Adolesc Health. 2024;74(4):801–807. https://doi.org/10.1016/j.jadohealth.2023.10.028

123. Carmichael P, Butler G, Masic U, et al. Short-term outcomes of pubertal suppression in a selected cohort of 12 to 15 year old young people with persistent gender dysphoria in the UK. PLoS One. 2021;16(2):e0243894. https://doi.org/10.1371/journal.pone.0243894

124. Mejia-Otero JD, White P, Lopez X. Effectiveness of puberty suppression with gonadotropin-releasing hormone agonists in transgender youth. Transgender Health. 2021;6(1):31–35. https://doi.org/10.1089/trgh.2020.0007

125. Navabi B, Tang K, Khatchadourian K, Lawson ML. Pubertal suppression, bone mass, and body composition in youth with gender dysphoria. Pediatrics. 2021;148(4):e2020039339. https://doi.org/10.1542/peds.2020-039339

126. Olson-Kennedy J, Streeter LH, Garofalo R, Chan YM, Rosenthal SM. Histrelin implants for suppression of puberty in youth with gender dysphoria: A comparison of 50 mcg/day (Vantas) and 65 mcg/day (SupprelinLA). Transgender Health. 2021;6(1):36–42. https://doi.org/10.1089/trgh.2020.0055

127. Russell I, Pearson B, Masic U. A longitudinal study of features associated with autism spectrum in clinic referred, gender diverse adolescents accessing puberty suppression treatment. J Autism Dev Disord. 2021;51(6):2068–2076. https://doi.org/10.1007/s10803-020-04698-8

128. Schulmeister C, Millington K, Kaufman M, et al. Growth in transgender/gender-diverse youth in the first year of treatment with gonadotropin-releasing hormone agonists. J Adolesc Health. 2022;70(1):108–113. https://doi.org/10.1016/j.jadohealth.2021.06.022

129. Ni J, Chi C, Aye T. Review of implant gonadotrophin-releasing hormone agonist use: Experience in a single academic center. Horm Res Paediatr. 2023;96(5):523–526. https://doi.org/10.1159/000529733

130. Mak A, Hwang R, Nace G, Jr, Allukian M, 3rd, Nance ML. Trends in histrelin implantation at a pediatric tertiary care center. J Surg Res. 2023;291:73–79. https://doi.org/10.1016/j.jss.2023.05.019

131. Pine-Twaddell E, Newfield RS, Marinkovic M. Extended use of histrelin implant in pediatric patients. Transgender Health. 2023;8(3):264–272. https://doi.org/10.1089/trgh.2021.0130

132. Roberge S, Roberge T, Corathers S, Nasomyont N. Determinants of bone mass accrual in transgender and gender diverse youth undergoing pubertal suppression therapy. J Clin Densitom Off J Int Soc Clin Densitom. 2024;27(3):101505. https://doi.org/10.1016/j.jocd.2024.101505

133. McPherson S, Freedman DEP. Psychological outcomes of 12–15-year-olds with gender dysphoria receiving pubertal suppression in the UK: Assessing reliable and clinically significant change. J Sex Marital Ther. 2024;50(3):315–325. https://doi.org/10.1080/0092623X.2023.2281986

134. Dominguez-Riscart J, Triviño-García A, Sanchez-Toscano E, et al. Voice self-perception and acoustic parameters in transgirls adolescent related to pubertal stage blockage. Early Hum Dev. 2025;201:106190. https://doi.org/10.1016/j.earlhumdev.2024.106190

135. Hobson BJ, Lett E, Hawkins LA, Swendiman RA, Nance ML, Dowshen NL. Transgender youth experiences with implantable GnRH agonists for puberty suppression. Transgender Health. 2022;7(4):364–368. https://doi.org/10.1089/trgh.2021.0006

136. Fuqua JS, Shi E, Eugster EA. A retrospective review of the use of bicalutamide in transfeminine youth; a single center experience. Int J Transgender Health. 2023;25(3):533–537. https://doi.org/10.1080/26895269.2023.2294321

137. Ciancia S, Dubois V, Craen M, et al. Effects of puberty suppression on bone, body composition, handgrip strength and glucolipid profile in early-pubertal transgender adolescents. Int J Transgender Health. 2025;26(3):861–873. https://doi.org/10.1080/26895269.2024.2353224

138. Nos AL, Klein DA, Adirim TA, et al. Association of gonadotropin-releasing hormone analogue use with subsequent use of gender-affirming hormones among transgender adolescents. JAMA Netw Open. 2022;55(11):e2239758. https://doi.org/10.1001/jamanetworkopen.2022.39758

139. Van Heesewijk J, Steenwijk MD, Kreukels BPC, Veltman DJ, Bakker J, Burke SM. Alterations in the inferior fronto-occipital fasciculus – A specific neural correlate of gender incongruence? Psychol Med. 2023;53(8):3461–3470. https://doi.org/10.1017/S0033291721005547

140. Nokoff NJ, Scarbro SL, Moreau KL, et al. Body composition and markers of cardiometabolic health in transgender youth on gonadotropin-releasing hormone agonists. Transgender Health. 2021;6(2):111–119. https://doi.org/10.1089/trgh.2020.0029

141. Vrouenraets LJJJ, De Vries MC, Hein IM, Arnoldussen M, Hannema SE, De Vries ALC. Perceptions on the function of puberty suppression of transgender adolescents who continued or discontinued treatment, their parents, and clinicians. Int J Transgender Health. 2021;23(4):428–441. https://doi.org/10.1080/26895269.2021.1974324

142. Fisher AD, Ristori J, Romani A, et al. Back to the future: Is GnRHa treatment in transgender and gender diverse adolescents only an extended evaluation phase? J Clin Endocrinol Metab. 2024;109(6):1565–1579. https://doi.org/10.1210/clinem/dgad729

143. Lahaije FAH, Van Setten PA, Levels W, Becking-Malpasso K, Claahsen-van der Grinten HL. GnRH analogs as a monotherapy in transgender and gender-diverse adolescents: Clinical insights from a single-center study. Endocr Connect. 2025;14(8):e250292. https://doi.org/10.1530/EC-25-0292

144. Karamanis G, Frisell T, Holmberg M, et al. Incidence of idiopathic intracranial hypertension in individuals with gonadotropin-releasing hormone analogue treatment for gender dysphoria in Sweden. JAMA Pediatr. 2023;177(7):726–727. https://doi.org/10.1001/jamapediatrics.2023.0656

145. Millington K, Finlayson C, Olson-Kennedy J, Garofalo R, Rosenthal SM, Chan YM. Association of high-density lipoprotein cholesterol with sex steroid treatment in transgender and gender-diverse youth. JAMA Pediatr. 2021;175(5):520–521. https://doi.org/10.1001/jamapediatrics.2020.5620

146. Mullins ES, Geer R, Metcalf M, et al. Thrombosis risk in transgender adolescents receiving gender-affirming hormone therapy. Pediatrics. 2021;147(4):e2020023549. https://doi.org/10.1542/peds.2020-023549

147. Sumerwell C, Carlin K, Walsh E, Hodax JK. Serum hormone concentrations in transgender youth receiving estradiol. Endocr Pract. 2024;30(2):155–159. https://doi.org/10.1016/j.eprac.2023.11.011

148. Taillefer V, Kelley J, Marsolais S, Chiniara L, Chadi N. Expected vs. perceived effects of gender-affirming hormone therapy among transmasculine adolescents. J Pediatr Endocrinol Metab. 2023;36(11):1072–1078. https://doi.org/10.1515/jpem-2023-0119

149. Valentine A, Nokoff N, Bonny A, et al. Cardiometabolic parameters among transgender adolescent males on testosterone therapy and body mass index-matched cisgender females. Transgender Health. 2021;6(6):369–373. https://doi.org/10.1089/trgh.2020.0052

150. Millington K, Lee JY, Olson-Kennedy J, Garofalo R, Rosenthal SM, Chan YM. Laboratory changes during gender-affirming hormone therapy in transgender adolescents. Pediatrics. 2024;153(5):e2023064380. https://doi.org/10.1542/peds.2023-064380

151. Millington K, Barrera E, Daga A, et al. The effect of gender-affirming hormone treatment on serum creatinine in transgender and gender-diverse youth: Implications for estimating GFR. Pediatr Nephrol. 2022;37(9):2141–2150. https://doi.org/10.1007/s00467-022-05445-0

152. Glintborg D, Møller JJK, Rubin KH, Christensen LL, Andersen MS. Autoimmune diseases in 3812 Danish transgender persons and 38 120 cisgender controls before and after transgender care: A register-based cohort study. Eur J Endocrinol. 2025;192(4):408–417. https://doi.org/10.1093/ejendo/lvaf051

153. Boskey E, Scheffey KL, Pilcher S, et al. A retrospective cohort study of transgender adolescents' gender-affirming hormone discontinuation. J Adolesc Health. 2025;76(4):584–591. https://doi.org/10.1016/j.jadohealth.2024.11.002

154. Gupta P, Patterson BC, Chu L, et al. Adherence to gender affirming hormone therapy in transgender adolescents and adults: A retrospective cohort study. J Clin Endocrinol Metab. 2023;108(11):e1236–1244. https://doi.org/10.1210/clinem/dgad306

155. McCallion S, Smith S, Kyle H, Shaikh MG, Wilkinson G, Kyriakou A. An appraisal of current service delivery and future models of care for young people with gender dysphoria. Eur J Pediatr. 2021;180(9):2969–2976. https://doi.org/10.1007/s00431-021-04075-2

156. Roberts CM, Klein DA, Adirim TA, Schvey NA, Hisle-Gorman E. Continuation of gender-affirming hormones among transgender adolescents and adults. J Clin Endocrinol Metab. 2022;107(9):e3937–3943. https://doi.org/10.1210/clinem/dgac251

157. Millington K, Chan YM. Lipoprotein subtypes after testosterone therapy in transmasculine adolescents. J Clin Lipidol. 2021;15(6):840–844. https://doi.org/10.1016/j.jacl.2021.09.051

158. Morningstar M, Thomas P, Anderson AM, et al. Exogenous testosterone administration is associated with differential neural response to unfamiliar peer's and own caregiver's voice in transgender adolescents. Dev Cogn Neurosci. 2023;59:101194. https://doi.org/10.1016/j.dcn.2022.101194

159. Grannis C, Mattson WI, Leibowitz SF, et al. Expanding upon the relationship between gender-affirming hormone therapy, neural connectivity, mental health, and body image dissatisfaction. Psychoneuroendocrinology. 2023;156:106319. https://doi.org/10.1016/j.psyneuen.2023.106319

160. Grannis C, Leibowitz SF, Gahn S, et al. Testosterone treatment, internalizing symptoms, and body image dissatisfaction in transgender boys. Psychoneuroendocrinology. 2021;132:105358. https://doi.org/10.1016/j.psyneuen.2021.105358

161. Campbell T, Mann S, Nguyen DH, Van der Meulen Rodgers Y. Hormone therapy, suicidal risk, and transgender youth in the United States. AEA Pap Proc Am Econ Assoc. 2023;113:551–555. https://doi.org/10.1257/pandp.20231057

162. Green AE, DeChants JP, Price MN, Davis CK. Association of gender-affirming hormone therapy with depression, thoughts of suicide, and attempted suicide among transgender and nonbinary youth. J Adolesc Health. 2022;70(4):643–649. https://doi.org/10.1016/j.jadohealth.2021.10.036

163. MacKinnon KR, Jeyabalan T, Strang JF, et al. Discontinuation of gender-affirming medical treatments: Prevalence and associated features in a nonprobabilistic sample of transgender and gender-diverse adolescents and young adults in Canada and the United States. J Adolesc Health. 2024;75(4):569–577. https://doi.org/10.1016/j.jadohealth.2024.05.015

164. Turban JL, King D, Kobe J, Reisner SL, Keuroghlian AS. Access to gender-affirming hormones during adolescence and mental health outcomes among transgender adults. PLoS One. 2022;17(1):e0261039. https://doi.org/10.1371/journal.pone.0261039

165. Baines HK, Connelly KJ. A prospective comparison study of subcutaneous and intramuscular testosterone injections in transgender male adolescents. J Pediatr Endocrinol Metab. 2023;36(11):1028–1036. https://doi.org/10.1515/jpem-2023-0237

166. Chen D, Berona J, Chan YM, et al. Psychosocial functioning in transgender youth after 2 years of hormones. N Engl J Med. 2023;388(3):240–250. https://doi.org/10.1056/NEJMoa2206297

167. Chu L, Gold S, Harris C, et al. Incidence and factors associated with acne in transgender adolescents on testosterone: A retrospective cohort study. Endocr Pract. 2023;29(5):353–355. https://doi.org/10.1016/j.eprac.2023.02.002

168. Cuéllar-Flores I, Martín-Bejarano M, García-Ron A, Villanueva S, Arias-Vivas E, López-de Lara D. Efectos del tratamiento con andrógenos sobre la neurocognición en adolescentes transgénero de mujer a hombre [Androgen treatment effects on neurocognition in female-to-male transgender adolescents]. Rev Neurol. 2024;78(3):83–89. https://doi.org/10.33588/rn.7803.2023207

169. Hranilovich JA, Millington K. Headache prevalence in transgender and gender diverse youth: A single-center case-control study. Headache. 2023;63(4):517–522. https://doi.org/10.1111/head.14493

170. Laurenzano SE, Newfield RS, Lee E, Marinkovic M. Subcutaneous testosterone is effective and safe as gender-affirming hormone therapy in transmasculine and gender-diverse adolescents and young adults: A single center's 8-year experience. Transgender Health. 2021;6(6):343–352. https://doi.org/10.1089/trgh.2020.0103

171. Moussaoui D, Hoq M, Elder CV, Grover SR, O'Connell MA, Pang KC. Is there an association between pelvic pain and gender-affirming testosterone therapy in trans masculine adolescents? An exploratory cross-sectional study. Int J Transgender Health. 2024;27(2):636–646. https://doi.org/10.1080/26895269.2024.2392685

172. Moussaoui D, Elder CV, O'Connell MA, Mclean A, Grover SR, Pang KC. Pelvic pain in transmasculine adolescents receiving testosterone therapy. Int J Transgend Health. 2022;25(1):10–18. https://doi.org/10.1080/26895269.2022.2147118

173. Baskaran C, Roberts SA, Barrera E, Pilcher S, Kumar R. Venous thromboembolism in transgender and gender non-binary youth is rare and occurs in the setting of secondary risk factors: A retrospective cohort study. Pediatr Blood Cancer. 2024;71(11):e31284. https://doi.org/10.1002/pbc.31284

174. Boogers L, Wiepjes CM, Klink DT, et al. Transgender girls grow tall: Adult height is unaffected by GnRH analogue and estradiol treatment. J Clin Endocrinol Metab. 2022;107(9):e3805–e3815. https://doi.org/10.1210/clinem/dgac349

175. Boogers LS, Van der Loos MATC, Wiepjes CM, Van Trotsenburg ASP, Den Heijer M, Hannema SE. The dose-dependent effect of estrogen on bone mineral density in trans girls. Eur J Endocrinol. 2023;189(2):290–296. https://doi.org/10.1093/ejendo/lvad116

176. Boogers LS, Reijtenbagh SJP, Wiepjes CM, Van Trotsenburg ASP, Den Heijer M, Hannema SE. Time course of body composition changes in transgender adolescents during puberty suppression and sex hormone treatment. J Clin Endocrinol Metab. 2024;109(8):e1593–e1601. https://doi.org/10.1210/clinem/dgad750

177. Boogers LS, McDonnell ESF, De Vries ALC, et al. Feminine figures: Body image and physical characteristics in trans women after puberty suppression and subsequent estradiol therapy. J Sex Med. 2025;22(10):1902–1909. https://doi.org/10.1093/jsxmed/qdaf206

178. Boogers LS, Sardo Infirri SA, Bouchareb A, et al. Variations in volume: Breast size in trans women in relation to timing of testosterone suppression. J Clin Endocrinol Metab. 2025;110(5):e1404–e1410. https://doi.org/10.1210/clinem/dgae573

179. Boogers L, Sikma BT, Bouman MB, et al. Shaping the skeleton: Impact of GnRH analogue and sex hormone therapy on skeletal dimensions in transgender individuals. J Clin Endocrinol Metab. 2025;110(5):e1411–e1419. https://doi.org/10.1210/clinem/dgae574

180. Butler G, Adu-Gyamfi K, Clarkson K, et al. Discharge outcome analysis of 1089 transgender young people referred to paediatric endocrine clinics in England 2008–2021. Arch Dis Child. 2022;107(1):1018–1022. https://doi.org/10.1136/archdischild-2022-324302

181. Chelliah P, Lau M, Kuper LE. Changes in gender dysphoria, interpersonal minority stress, and mental health among transgender youth after one year of hormone therapy. J Adolesc Health. 2024;74(6):1106–1111. https://doi.org/10.1016/j.jadohealth.2023.12.024

182. Ciancia S, Klink D, Craen M, Cools M. Early puberty suppression and gender-affirming hormones do not alter final height in transgender adolescents. Eur J Endocrinol. 2023;189(3):396–401. https://doi.org/10.1093/ejendo/lvad125

183. Cohen A, Gomez-Lobo V, Willing L, et al. Shifts in gender-related medical requests by transgender and gender-diverse adolescents. J Adolesc Health. 2023;72(3):428–436. https://doi.org/10.1016/j.jadohealth.2022.10.020

184. Crabtree L, Connelly KJ, Guerriero J, et al. A more nuanced story: Pediatric gender-affirming healthcare is associated with satisfaction and confidence. J Adolesc Health. 2024;75(5):772–779. https://doi.org/10.1016/j.jadohealth.2024.06.016

185. De Castro C, Solerdelcoll M, Plana MT, et al. High persistence in Spanish transgender minors: 18 years of experience of the Gender Identity Unit of Catalonia. Span J Psychiatry Ment Health. 2024;17(1):35–40. https://doi.org/10.1016/j.rpsm.2022.02.001

186. Eitel KB, Hodax JK, DiVall S, Kidd KM, Salehi P, Sequeira GM. Leuprolide acetate for puberty suppression in transgender and gender diverse youth: A comparison of subcutaneous Eligard versus intramuscular Lupron. J Adolesc Health. 2023;72(2):307–311. https://doi.org/10.1016/j.jadohealth.2022.09.017

187. Elkadi J, Chudleigh C, Maguire AM, Ambler GR, Scher S, Kozlowska K. Developmental pathway choices of young people presenting to a gender service with gender distress: A prospective follow-up study. Children. 2023;10(2):314. https://doi.org/10.3390/children10020314

188. Finegan JL, Marinkovic M, Okamuro K, Newfield RS, Anger JT. Experience with gender affirming hormones and puberty blockers (gonadotropin releasing hormone agonist): A qualitative analysis of sexual function. J Sex Med. 2025;22(5):945–950. https://doi.org/10.1093/jsxmed/qdaf061

189. Glintborg D, Møller JJK, Rubin KH, et al. Gender-affirming treatment and employment rate in 3812 Danish transgender persons and 38 120 controls. J Clin Endocrinol Metab. 2024;109(12):3076–3086. https://doi.org/10.1210/clinem/dgae351

190. Grimstad F, Knoll MM, Jacobson JD. Oxandrolone use in trans-masculine youth appears to increase adult height: Preliminary evidence. LGBT Health. 2021;8(4):300–306. https://doi.org/10.1089/lgbt.2020.0355

191. Grimstad F, Kremen J, Shim J, Charlton BM, Boskey E. Breakthrough bleeding in transgender and gender diverse adolescents and young adults on long-term testosterone. J Pediatr Adolesc Gynecol. 2021;34(5):706–716. https://doi.org/10.1016/j.jpag.2021.04.004

192. Hisle-Gorman E, Schvey NA, Adirim TA, et al. Mental healthcare utilization of transgender youth before and after affirming treatment. J Sex Med. 2021;18(8):1444–1454. https://doi.org/10.1016/j.jsxm.2021.05.014

193. Kain EJ, Fuqua JS, Eugster EA. A retrospective study of the use of gonadotropin-releasing hormone analogs and testosterone in transgender boys: Who, what, when, and for how long? Transgender Health. 2024;9(4):357–360. https://doi.org/10.1089/trgh.2022.0156

194. Lavender R, Shaw S, Maninger JK, et al. Impact of hormone treatment on psychosocial functioning in gender-diverse young people. LGBT Health. 2023;10(5):382–390. https://doi.org/10.1089/lgbt.2022.0201

195. Marwa A, Misra M, Lopez X. Determinants of bone mineral density in transgender youth. Transgender Health. 2022;7(3):213–218. https://doi.org/10.1089/trgh.2020.0111

196. Mellin CS, Braun M, Walch A, et al. Pediatric gender diversity beyond the binary: An exploration of gender-affirming care for nonbinary and genderqueer youth seen over time at a single institution gender center. Transgender Health. 2024;9(2):107–117. https://doi.org/10.1089/trgh.2021.0199

197. Nokoff NJ, Bothwell S, Rice JD, et al. Insulin sensitivity, body composition and bone mineral density after testosterone treatment in transgender youth with and without prior GnRH agonist therapy. J Clin Transl Endocrinol. 2024;36:100356. https://doi.org/10.1016/j.jcte.2024.100356

198. Nokoff NJ, DuBose L, Bothwell S, et al. Impact of testosterone on endothelial function varies by GnRH agonist treatment. J Endocr Soc. 2025;9(7):bvaf086. https://doi.org/10.1210/jendso/bvaf086

199. Nokoff NJ, Nemkov T, Bothwell S, et al. Differences in cardiorespiratory fitness by gonadotropin-releasing hormone agonist treatment before and after testosterone in transgender adolescents. J Appl Physiol Bethesda Md 1985. 2024;137(5):1470–1483. https://doi.org/10.1152/japplphysiol.00629.2024

200. Nunes-Moreno M, Furniss A, Cortez S, et al. Mental health diagnoses and suicidality among transgender youth in hospital settings. LGBT Health. 2025;12(1):20–28. https://doi.org/10.1089/lgbt.2023.0394

201. Olson KR, Raber GF, Gallagher NM. Levels of satisfaction and regret with gender-affirming medical care in adolescence. JAMA Pediatr. 2024;178(12):1354–1361. https://doi.org/10.1001/jamapediatrics.2024.4527

202. Olson-Kennedy J, Wang L, Wong CF, et al. Emotional health of transgender youth 24 months after initiating gender-affirming hormone therapy. J Adolesc Health. 2025;77(1):41–50. https://doi.org/10.1016/j.jadohealth.2024.11.014

203. Karakılıç-Özturan E, Öztürk AP, Baş F, et al. Endocrinological approach to adolescents with gender dysphoria: Experience of a pediatric endocrinology department in a tertiary center in Turkey. J Clin Res Pediatr Endocrinol. 2023;15(3):276–284. https://doi.org/10.4274/jcrpe.galenos.2023.2023-1-13

204. Perl L, Segev-Becker A, Israeli G, Elkon-Tamir E, Oren A. Blood pressure dynamics after pubertal suppression with gonadotropin-releasing hormone analogs followed by testosterone treatment in transgender male adolescents: A pilot study. LGBT Health. 2020;7(6):340–344. https://doi.org/10.1089/lgbt.2020.0026

205. Persky RW, Apple D, Dowshen N, et al. Pubertal suppression in early puberty followed by testosterone mildly increases final height in transmasculine youth. J Endocr Soc. 2024;8(6):bvae089. https://doi.org/10.1210/jendso/bvae089

206. Pham A, Kerman H, Albertson K, Crouch JM, Inwards-Breland DJ, Ahrens KR. Understanding the complex relationship between one's body, eating, exercise, and gender-affirming medical care among transgender and nonbinary adolescents and young adults. Transgender Health. 2023;8(2):149–158. https://doi.org/10.1089/trgh.2021.0112

207. Roy MK, Bothwell S, Kelsey MM, et al. Bone density in transgender youth on gender-affirming hormone therapy. J Endocr Soc. 2024;8(5):bvae045. https://doi.org/10.1210/jendso/bvae045

208. Strang JF, Chen D, Nelson E, et al. Transgender youth executive functioning: Relationships with anxiety symptoms, autism spectrum disorder, and gender-affirming medical treatment status. Child Psychiatry Hum Dev. 2022;53(6):1252–1265. https://doi.org/10.1007/s10578-021-01195-6

209. Tordoff DM, Wanta JW, Collin A, Stepney C, Inwards-Breland DJ, Ahrens K. Mental health outcomes in transgender and nonbinary youths receiving gender-affirming care. JAMA Netw Open. 2022;5(2):e220978. https://doi.org/10.1001/jamanetworkopen.2022.0978

210. Valentine A, Davis S, Furniss A, et al. Multicenter analysis of cardiometabolic-related diagnoses in transgender and gender-diverse youth: A PEDSnet study. J Clin Endocrinol Metab. 2022;107(10):e4004–e4014. https://doi.org/10.1210/clinem/dgac469

211. Van der Loos MATC, Hellinga I, Vlot MC, Klink DT, Den Heijer M, Wiepjes CM. Development of hip bone geometry during gender-affirming hormone therapy in transgender adolescents resembles that of the experienced gender when pubertal suspension is started in early puberty. J Bone Miner Res Off J Am Soc Bone Miner Res. 2021;36(5):931–941. https://doi.org/10.1002/jbmr.4262

212. Van der Loos MATC, Hannema SE, Klink D, Den Heijer M, Wiepjes CM. Continuation of gender-affirming hormones in transgender people starting puberty suppression in adolescence: A cohort study in the Netherlands. Lancet Child Adolesc Health. 2022;6(12):869–875. https://doi.org/10.1016/S2352-4642(22)00254-1

213. Van der Loos MATC, Klink DT, Hannema SE, et al. Children and adolescents in the Amsterdam Cohort of Gender Dysphoria: Trends in diagnostic- and treatment trajectories during the first 20 years of the Dutch Protocol. J Sex Med. 2023;20(3):398–409. https://doi.org/10.1093/jsxmed/qdac029

214. Van der Loos MATC, Vlot MC, Klink DT, Hannema SE, Den Heijer M, Wiepjes CM. Bone mineral density in transgender adolescents treated with puberty suppression and subsequent gender-affirming hormones. JAMA Pediatr. 2023;177(12):1332. https://doi.org/10.1001/jamapediatrics.2023.4588

215. Van der Meulen IS, Arnoldussen M, Van der Miesen AIR, et al. Sexual satisfaction and dysfunction in transgender adults following puberty suppression treatment during adolescence. J Sex Med. 2025;22(8):1493–1503. https://doi.org/10.1093/jsxmed/qdaf095

216. Waldner RC, Doulla M, Atallah J, Rathwell S, Grimbly C. Leuprolide acetate and QTc interval in gender-diverse youth. Transgender Health. 2023;8(1):84–88. https://doi.org/10.1089/trgh.2021.0102

217. White AA, Pearce T, Coenen I, et al. Plasma testosterone concentration is correlated with circulating immune cell abundance in transgender young people on gender-affirming hormone treatment. Front Immunol. 2025;16:1608543. https://doi.org/10.3389/fimmu.2025.1608543

218. Willemsen LA, Boogers LS, Wiepjes CM, et al. Just as tall on testosterone; a neutral to positive effect on adult height of GnRHa and testosterone in trans boys. J Clin Endocrinol Metab. 2023;108(2):414–421. https://doi.org/10.1210/clinem/dgac571

219. Wittlin NM, Gallagher NM, Atwood S, Olson KR. Mental health during medical transition in a US and Canadian sample of early socially transitioned transgender youth. J Adolesc Health. 2025;76(2):228–237. https://doi.org/10.1016/j.jadohealth.2024.10.023

220. Zaitoon H, Kapusta L, Israeli G, et al. QT interval changes in transgender/gender diverse adolescents receiving gonadotropin-releasing hormone agonist and gender-affirming hormonal treatment. Int J Transgender Health. 2025;27(2):1033–1044. https://doi.org/10.1080/26895269.2025.2503219

221. Abernathey L, Ryan ME, Golub S, et al. Long-acting reversible contraception in gender-diverse adolescents and young adults: Outcomes from a multisite collaborative. Contraception. 2023;127:110131. https://doi.org/10.1016/j.contraception.2023.110131

222. Alaniz VI, Sheeder JL, Whitmore GT, et al. Menstrual suppression in adolescent and young adult transgender males. J Pediatr Adolesc Gynecol. 2023;36(2):116–121. https://doi.org/10.1016/j.jpag.2022.10.007

223. Moussaoui D, O'Connell MA, Elder CV, Grover SR, Pang KC. Characteristics of menstrual suppression and its association with mental health in transgender adolescents. Obstet Gynecol. 2023;142(5):1096–1104. https://doi.org/10.1097/aog.0000000000005317

224. Scatoni A, Roberts Z, Boskey ER, et al. Danazol's use for menstrual suppression in transgender individuals: A retrospective multi-site cohort study. Women's Health. 2024;20:17455057241265081. https://doi.org/10.1177/17455057241265081

225. Schwartz BI, Bear B, Short VL, Kazak AE. Outcomes of menstrual management use in transgender and gender-diverse adolescents. Obstet Gynecol. 2023;141(4):748–755. https://doi.org/10.1097/AOG.0000000000005123

226. Amir H, Perl L, Barda S, et al. Adolescent transgender females present impaired semen quality that is suitable for intracytoplasmic sperm injection even before initiating gender-affirming hormone treatment. Reprod Sci. 2022;29(1):260–269. https://doi.org/10.1007/s43032-021-00561-y

227. Aslam M, Norup PB, Haahr ME, et al. Semen cryopreservation and semen quality in transfeminine adolescents prior to hormone therapy. J Endocr Soc. 2025;9(8):bvaf105. https://doi.org/10.1210/jendso/bvaf105

228. Asseler JD, De Nie I, Van Rooij FB, et al. Transgender persons' view on previous fertility decision-making and current infertility: A qualitative study. Hum Reprod. 2024;39(9):2032–2042. https://doi.org/10.1093/humrep/deae155

229. Barrera E, Locks R, Kremen J, Yu R. Fertility preservation in transfeminine adolescents using TESE at the time of Histrelin Acetate subcutaneous implant placement: A case series. J Pediatr Urol. 2023;19(5):e1–e540. https://doi.org/10.1016/j.jpurol.2023.02.006

230. Barrett F, Shaw J, Blakemore JK, Fino ME. Fertility preservation for adolescent and young adult transmen: A case series and insights on oocyte cryopreservation. Front Endocrinol. 2022;13:873508. https://doi.org/10.3389/fendo.2022.873508

231. Cooper HC, Long J, Aye T. Fertility preservation in transgender and non-binary adolescents and young adults. PLoS One. 2022;17(3):e0265043. https://doi.org/10.1371/journal.pone.0265043

232. Cromack SC, Walter JR, Smith KN, Elvikis J, Bazzetta SE, Goldman KN. Oocyte cryopreservation in transgender and gender-diverse individuals with or without prior testosterone use. Obstet Gynecol. 2024;144(6):e121–e124. https://doi.org/10.1097/AOG.0000000000005749

233. De Nie I, Mulder CL, Meißner A, et al. Histological study on the influence of puberty suppression and hormonal treatment on developing germ cells in transgender women. Hum Reprod Oxf Engl. 2022;37(2):297–308. https://doi.org/10.1093/humrep/deab240

234. De Nie I, Asseler JD, Arnoldussen M, et al. Reflecting on the importance of family building and fertility preservation: Transgender people's experiences with starting gender-affirming treatment as an adolescent. Transgender Health. 2024;9(4):298–306. https://doi.org/10.1089/trgh.2022.0135

235. Dilday EA, Bukulmez O, Saner K, Lopez X, Jarin J. Sperm cryopreservation outcomes in transgender adolescents compared with adolescents receiving gonadotoxic therapy. Transgender Health. 2022;7(6):528–532. https://doi.org/10.1089/trgh.2021.0037

236. Komorowski AS, Fisher AR, Jungheim ES, Lewis CS, Omurtag KR. Fertility preservation discussions, referral and follow-up in male-to-female and female-to-male adolescent transgender patients. Hum Fertil. 2023;26(5):903–907. https://doi.org/10.1080/14647273.2021.2015804

237. Parikh N, Chattha A, Fredrickson JR, et al. The importance of fertility preservation in the transgender population. Urology. 2025;195:91–95. https://doi.org/10.1016/j.urology.2024.08.020

238. Peri A, Ahler A, Gook D, et al. Predicting successful sperm retrieval in transfeminine adolescents after testicular biopsy. J Assist Reprod Genet. 2021;38(10):2735–2743. https://doi.org/10.1007/s10815-021-02293-z

239. Pierce A, Holden M, Pham A, Lucidi R, New EP. An intervention to increase fertility preservation counseling prior to starting gender-affirming hormone therapy. J Pediatr Adolesc Gynecol. 2025;38(4):492–497. https://doi.org/10.1016/j.jpag.2025.01.173

240. Ralph P, Mahoud M, Schlager D, et al. United Kingdom data collection of semen quality in transgender adolescent females seeking fertility preservation. Fertil Steril. 2025;123(2):313–321. https://doi.org/10.1016/j.fertnstert.2024.09.006

241. Stolk THR, Van Mello NM, Meißner A, Huirne JAF, Van den Boogaard E. The experience of transfeminine adolescents and their parents regarding fertility preservation via testicular sperm extraction (TESE): A qualitative study. Hum Reprod. 2024;39(11):2512–2524. https://doi.org/10.1093/humrep/deae200

242. Aquino NJ, Boskey ER, Staffa SJ, et al. A single center case series of gender-affirming surgeries and the evolution of a specialty anesthesia team. J Clin Med. 2022;11(7):1943. https://doi.org/10.3390/jcm11071943

243. Ascha M, Sasson DC, Sood R, et al. Top surgery and chest dysphoria among transmasculine and nonbinary adolescents and young adults. JAMA Pediatr. 2022;176(11):1115–1122. https://doi.org/10.1001/jamapediatrics.2022.3424

244. Diaddigo SE, Asadourian PA, Lavalley MN, Marano AA, Rohde CH. Masculinizing chest reconstruction in adolescents and young adults: An analysis of National Surgical Quality Improvement Program data: An analysis of National Surgical Quality Improvement Program data. Ann Plast Surg. 2024;92(2):253–257. https://doi.org/10.1097/SAP.0000000000003735

245. Hassan B, Zeitouni F, Ascha M, Sanders R, Liang F. Temporal trends in gender affirmation surgery among transgender and non-binary minors. Cureus. 2023;15(9):e45948. https://doi.org/10.7759/cureus.45948

246. Hassan B, Zeitouni F, Ascha M, et al. Breast surgery in adolescents: Cisgender breast reduction versus transgender and nonbinary chest masculinization: Cisgender breast reduction versus transgender and nonbinary chest masculinization. Ann Plast Surg. 2024;93(2):194–199. https://doi.org/10.1097/SAP.0000000000003981

247. Mehringer JE, Harrison JB, Quain KM, Shea JA, Hawkins LA, Dowshen NL. Experience of chest dysphoria and masculinizing chest surgery in transmasculine youth. Pediatrics. 2021;147(3):e2020013300. https://doi.org/10.1542/peds.2020-013300

248. Skorochod R, Rysin R, Wolf Y. Age-related outcomes of chest masculinization surgery: A single-surgeon retrospective cohort study. Plast Reconstr Surg Glob Open. 2023;11(2):e4799. https://doi.org/10.1097/GOX.0000000000004799

249. Tang A, Hojilla JC, Jackson JE, et al. Gender-affirming mastectomy trends and surgical outcomes in adolescents. Ann Plast Surg. 2022;88(4 Suppl):S325–S331. https://doi.org/10.1097/SAP.0000000000003135

250. Weixel T, Pellicane MJ, Ciesla JA, Wildman B, Medalie D. Post-operative outcomes for transmasculine and nonbinary individuals who received top surgery as minors. Int J Transgender Health. 2025;27(2):973–983. https://doi.org/10.1080/26895269.2025.2498751

251. Boskey ER, Jolly D, Kant JD, Ganor O. Prospective evaluation of psychosocial changes after chest reconstruction in transmasculine and non-binary youth. J Adolesc Health. 2023;73(5):503–509. https://doi.org/10.1016/j.jadohealth.2023.04.029

252. Ewing E, Sendek G, Becker M, et al. An assessment of the longitudinal impact of gender-affirming care in an adolescent and young adult transmasculine and nonbinary patient population. Plast Reconstr Surg Glob Open. 2025;13(6):e6911. https://doi.org/10.1097/GOX.0000000000006911

253. Arnoldussen M, Hooijman EC, Kreukels BPC, De Vries ALC. Association between pre-treatment IQ and educational achievement after gender-affirming treatment including puberty suppression in transgender adolescents. Clin Child Psychol Psychiatry. 2022;27(4):1069–1076. https://doi.org/10.1177/13591045221091652

254. Arnoldussen M, Van der Miesen AIR, Elzinga WS, et al. Self-perception of transgender adolescents after gender-affirming treatment: A follow-up study into young adulthood. LGBT Health. 2022;9(4):238–246. https://doi.org/10.1089/lgbt.2020.0494

255. Becker-Hebly I, Fahrenkrug S, Campion F, Richter-Appelt H, Schulte-Markwort M, Barkmann C. Psychosocial health in adolescents and young adults with gender dysphoria before and after gender-affirming medical interventions: A descriptive study from the Hamburg Gender Identity Service. Eur Child Adolesc Psychiatry. 2021;30(11):1755–1767. https://doi.org/10.1007/s00787-020-01640-2

256. Jessen RS, Wæhre A, David LW, Stänicke LI, Stänicke E. 'It was actually my family and friends who noticed that my voice changed': An interview study on the experiences of transgender and non-binary youth and young adults three years into medical treatment. Int J Transgender Health. 2025:1–15. https://doi.org/10.1080/26895269.2025.2478498

257. Nieder TO, Mayer TK, Hinz S, Fahrenkrug S, Herrmann L, Becker-Hebly I. Individual treatment progress predicts satisfaction with transition-related care for youth with gender dysphoria: A prospective clinical cohort study. J Sex Med. 2021;18(3):632–645. https://doi.org/10.1016/j.jsxm.2020.12.010

258. Nyquist CB, Torgersen L, David LW, Diseth TH, Gulbrandsen K, Waehre A. Treatment trajectories among children and adolescents referred to the Norwegian National Center for Gender Incongruence. Acta Paediatr Oslo Nor 1992. 2025;114(5):1006–1014. https://doi.org/10.1111/apa.17530

259. Reyes V, Loren D, Bocek K, Kahn NF, Kidd KM, Sequeira GM. 'I don't know if I would've made it through high school without it': Transgender adolescents' perspectives on the impact of gender-affirming care. Transgender Health. 2024;10(6):503–509. https://doi.org/10.1089/trgh.2024.0115

260. Van der Meulen IS, Bungener SL, Van der Miesen AIR, et al. Timing of puberty suppression in transgender adolescents and sexual functioning after vaginoplasty. J Sex Med. 2025;22(1):196–204. https://doi.org/10.1093/jsxmed/qdae152

261. Lee MK, Yih Y, Willis DR, Fogel JM, Fortenberry JD. The impact of gender affirming medical care during adolescence on adult health outcomes among transgender and gender diverse individuals in the United States: The role of state-level policy stigma. LGBT Health. 2024;11(2):111–121. https://doi.org/10.1089/lgbt.2022.0334

262. Julian JM, Salvetti B, Held JI, Murray PM, Lara-Rojas L, Olson-Kennedy J. The impact of chest binding in transgender and gender diverse youth and young adults. J Adolesc Health. 2021;68(6):1129–1134. https://doi.org/10.1016/j.jadohealth.2020.09.029

263. Abreu RL, Sostre JP, Gonzalez KA, Lockett GM, Matsuno E, Mosley DV. Impact of gender-affirming care bans on transgender and gender diverse youth: Parental figures' perspective. J Fam Psychol. 2022;36(5):643–652. https://doi.org/10.1037/fam0000987

264. Brandon-Friedman RA, Tabb A, Imburgia TM, et al. Perspectives of gender-diverse youth and caregivers facing gender-affirming medical intervention bans. LGBT Health. 2025;12(2):108–115. https://doi.org/10.1089/lgbt.2024.0079

265. DeChants JP, Price MN, Green AE, Davis CK, Pick CJ. Association of updating identification documents with suicidal ideation and attempts among transgender and nonbinary youth. Int J Environ Res Public Health. 2022;19(9):5016. https://doi.org/10.3390/ijerph19095016

266. Kennedy N. Harming children: The effects of the UK puberty blocker ban. J Gend Stud. 2025:1–17. https://doi.org/10.1080/09589236.2025.2521699

267. Miller-Jacobs C, Operario D, Hughto JMW. State-level policies and health outcomes in U.S. transgender adolescents: Findings from the 2019 youth risk behavior survey. LGBT Health. 2023;10(6):447–455. https://doi.org/10.1089/lgbt.2022.0247

268. Tan KKH, Byrne JL, Treharne GJ, Veale JF. Unmet need for gender-affirming care as a social determinant of mental health inequities for transgender youth in Aotearoa/New Zealand. J Public Health Oxf Engl. 2023;45(2):e225–e233. https://doi.org/10.1093/pubmed/fdac131

269. Haby MM, Chapman E, Clark R, Barreto J, Reveiz L, Lavis JN. What are the best methodologies for rapid reviews of the research evidence for evidence-informed decision making in health policy and practice: A rapid review. Health Res Policy Syst. 2016;14(1):83. https://doi.org/10.1186/s12961-016-0155-7

270. Nussbaumer-Streit B, Sommer I, Hamel C, et al. Rapid reviews methods series: Guidance on team considerations, study selection, data extraction and risk of bias assessment. BMJ Evid Based Med. 2023;28(6):418–423. https://doi.org/10.1136/bmjebm-2022-112185

271. Ashley F, Tordoff DM, Olson-Kennedy J, Restar AJ. Randomized-controlled trials are methodologically inappropriate in adolescent transgender healthcare. Int J Transgender Health. 2024;25(3):407–418. https://doi.org/10.1080/26895269.2023.2218357

272. Matheny Antommaria AH, Kelleher M, Peterson RJ. Quality of evidence and strength of recommendations in American Academy of Pediatrics' guidelines. Pediatrics. 2025;155(4):e2024067836. https://doi.org/10.1542/peds.2024-067836

273. Chong MC, Sharp MK, Smith SM, et al. Strong recommendations from low certainty evidence: A cross-sectional analysis of a suite of national guidelines. BMC Med Res Methodol. 2023;23(1):68. https://doi.org/10.1186/s12874-023-01895-8

274. Thomas ET, Thomas ST, Perera R, Gill PJ, Moloney S, Heneghan CJ. The quality of paediatric asthma guidelines: Evidence underpinning diagnostic test recommendations from a meta-epidemiological study. Fam Pract. 2024;41(4):460–469. https://doi.org/10.1093/fampra/cmad052

275. Carter B, Bray L, al-Najjar N, et al. The impact of parent treatment preference and other factors on recruitment: Lessons learned from a paediatric epilepsy randomised controlled trial. Trials. 2023;24:83. https://doi.org/10.1186/s13063-023-07091-9

276. Guyatt G, Vandvik PO, Iorio A, et al. Core GRADE 7: Principles for moving from evidence to recommendations and decisions. BMJ. 2025;389:e083867. https://doi.org/10.1136/bmj-2024-083867

277. Guyatt G, Brignardello-Petersen R, Ibrahim S, Roldán-Benitez Y, Couban R. Systematic reviews related to gender-affirming care [Academic] [homepage on the Internet]. 2025 [cited 2025 Nov 30]. Available from: https://hei.healthsci.mcmaster.ca/systematic-reviews-related-to-gender-affirming-care/

278. Republic of South Africa. Children's Act 38 of 2005 [homepage on the Internet]. c2005 [cited 2025 Sep 29]. Available from: https://www.gov.za/sites/default/files/gcis_document/201409/a38-053.pdf